# STIC Search Report
## Biotech-Chem Library

**STIC Database Tracking Number: 122905**

| | |
|---|---|
| **TO: Ralph J Gitomer**<br>**Location: 3d65 / 3e71**<br>**Tuesday, May 25, 2004**<br>**Art Unit: 1651**<br>**Phone: 272-0916**<br>**Serial Number: 10 / 083894** | **From: Jan Delaval**<br>**Location: Biotech-Chem Library**<br>**Rem 1A51**<br>**Phone: 272-2504**<br><br>**jan.delaval@uspto.gov** |

## Search Notes

JAN 122905

Access DB# _____

RECEIVED MAY 25 2005 (STIC)

# SEARCH REQUEST FORM

## Scientific and Technical Information Center

Requester's Full Name: R GITOMER Examiner # : _____ Date: 5/25/05

Art Unit: 1651 Phone Number 30 _____ Serial Number: 10/083,894

Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

3D65/3E71

**If more than one search is submitted, please prioritize searches in order of need.**

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

JAN

**********

**STAFF USE ONLY**

| | | | |
|---|---|---|---|
| Searcher: | | **Type of Search** | **Vendors and cost where applicable** |
| Searcher Phone #: | 22504 | NA Sequence (#) _____ | STN ✓ |
| Searcher Location: | | AA Sequence (#) _____ | Dialog _____ |
| Date Searcher Picked Up: | 5/25 | Structure (#) _____ | Questel/Orbit _____ |
| Date Completed: | 5/25 | Bibliographic ✓ | Dr.Link _____ |
| Searcher Prep & Review Time: | | Litigation _____ | Lexis/Nexis _____ |
| Clerical Prep Time: | 15 | Fulltext _____ | Sequence Systems _____ |
| Online Time: | 1105 | Patent Family _____ | WWW/Internet _____ |
| | | Other _____ | Other (specify) _____ |

PTO-1590 (8-01)

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=> d his

     (FILE 'HOME' ENTERED AT 13:34:50 ON 25 MAY 2004)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:34:58 ON 25 MAY 2004
L1           780 S ?FARNESYL?/CNS
L2           239 S L1 AND ?TRANSFERASE?/CNS
L3           541 S L1 NOT L2
L4           206 S L2 AND FARNES?/INS.HP
L5            33 S L2 NOT L4
L6            22 S L5 AND FARNESYLTRANSFERASE
L7            11 S L6 AND CYSTEINE
L8             6 S L7 NOT CANDIDA
L9           172 S L4 AND FARNESYLTRANSFERASE/INS.HP
L10           34 S L4 NOT L9
L11            5 S L10 AND FARNESYL PROTEIN TRANSFERASE
L12          183 S L9,L8,L11
L13           29 S L10 NOT L12
L14           29 S L4 NOT L12
L15           29 S L13,L14
L16            4 S L15 AND FARNESYL TRANSFERASE
L17            0 S L15 AND FARNESYLTRANSFERASE
L18            0 S L15 AND FARNESYL PROTEIN TRANSFERASE
L19          187 S L12,L16
L20           25 S L15 NOT L19
L21          593 S L1-L18,L20 NOT L19

     FILE 'HCAPLUS' ENTERED AT 13:42:56 ON 25 MAY 2004
L22         1800 S L19
L23         6717 S L21
L24         1909 S ?FARNESYLTRANSFERASE? OR ?FARNESYL PROTEIN TRANSFERASE?
L25          612 S FARNESYL TRANSFERASE
L26         8806 S L22-L25
L27          201 S L26 AND (DRUG SCREENING+OLD,NT,PFT OR DRUG DESIGN+OLD,NT,PFT)
                 E REISS Y/AU
L28           39 S E3,E4
                 E GOLDSTEIN J/AU
L29          257 S E3,E12,E13
                 E GOLDSTEIN JOE/AU
L30            4 S E3
L31          425 S E27,E28,E31
                 E BROWN M/AU
L32          263 S E3,E49
                 E BROWN MICHAEL/AU
L33          105 S E3
                 E BROWN MICHAEL S/AU
L34          448 S E3-E5
L35            8 S E16,E17
L36           41 S L26 AND L28-L35
L37            5 S L28-L35 AND (TKCVIM OR CVIM OR KKSKTKCVIM)
L38            5 S L28-L35 AND ?CVIM?
L39            5 S L37,L38

     FILE 'REGISTRY' ENTERED AT 13:50:31 ON 25 MAY 2004
                 E CVIM/SQEP
L40           29 S E3
                 E TKCVIM/SQEP
L41            2 S E3
                 E KKSKTKCVIM/SQEP
L42            3 S E3

     FILE 'HCAPLUS' ENTERED AT 13:51:24 ON 25 MAY 2004
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L43          45 S L40-L42
L44          30 S TKCVIM OR CVIM OR KKSKTKCVIM
L45          60 S L43,L44 AND L26
L46         137 S L26 AND P21RAS
L47          24 S L26 AND P21 RAS
L48        1361 S L26 AND RAS
L49         309 S L26 AND P21?
L50          26 S L36 AND L45,L46-L49
L51          26 S L39,L50
L52           1 S L51 AND L27
L53           5 S L51 AND SCREEN?
L54          18 S L51 AND INHIBIT?
L55          18 S L52-L54
L56          18 S L39,L55
L57          23 S L36 NOT L56
L58          18 S L56 AND (INHIBIT? OR BLOCK? OR ANTAGON? OR PREVENT?)
L59           5 S L58 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L60          13 S L58 NOT L59
L61           4 S (US20030170766 OR US5141851)/PN OR (US2000-665637# OR US92-93
L62           4 S L61 AND L22-L39,L43-L60
L63           5 S L59,L62
L64        8921 S L26 OR ?FARNESYL?(L)?TRANSFERASE?
L65        2692 S L64 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L66           6 S L65 AND L43,L44
L67          11 S L65 AND (P21? OR P21 RAS)
L68          13 S L65 AND RAS PROTEINS+OLD,NT,PFT/CT
L69           1 S L65 AND (DRUG SCREENING+OLD,NT,PFT OR DRUG DESIGN+OLD,NT,PFT)
L70         494 S L65 AND (INHIBIT? OR BLOCK? OR ANTAGON? OR PREVENT?)
L71          37 S L70 AND METHOD?
L72          48 S L63,L66-L69,L71
L73          16 S L72 AND ENZYM?/SC,SX
                SEL DN AN L73 7 12 13 14 16
L74          11 S L73 NOT E1-E15
L75          32 S L72 NOT L73
L76          11 S L74 AND (RAS OR P21? OR ?FARNES? OR ?TRANSFERASE? OR ?CVIM? O
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:14:41 ON 25 MAY 2004
L77          24 S E16-E39
L78          18 S L77 AND L1-L21
L79           6 S L77 AND L40-L42
L80           3 S L78 AND UNSPECIFIED NOT SQL/FA
L81          15 S L78 NOT L79,L80

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:16:43 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   24 MAY 2004  HIGHEST RN 685504-43-2
DICTIONARY FILE UPDATES:  24 MAY 2004  HIGHEST RN 685504-43-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.
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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L80 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN **131384-38-8** REGISTRY
CN **Farnesyltransferase, protein (cysteine) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **CAAX farnesyltransferase**
CN **Farnesyl protein transferase**
CN **Farnesyltransferase**
CN **Farnesyltransferase, farnesyl pyrophosphate-protein**
CN **Farnesyltransferase, protein**
CN **Prenylprotein transferase**
CN **Prenyltransferase**
CN **Protein cysteine farnesyltransferase**
CN **Protein farnesyltransferase**
CN **Protein prenyltransferase**
CN **Ras farnesyltransferase**
DR 132421-44-4, 56626-17-6, 133876-90-1
MF **Unspecified**
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CEN, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1666 REFERENCES IN FILE CA (1907 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1670 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:350520

REFERENCE 2: 140:349873

REFERENCE 3: 140:336357

REFERENCE 4: 140:333589

REFERENCE 5: 140:333562

REFERENCE 6: 140:321532

REFERENCE 7: 140:321011

REFERENCE 8: 140:315043

REFERENCE 9: 140:314552

REFERENCE 10: 140:314309

L80 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN **130731-20-3** REGISTRY
CN **Methyltransferase, protein C-terminal farnesylcysteine O- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **C-Terminal isoprenylcysteine methyltransferase**
CN E.C. 2.1.1.100
CN **Farnesyl cysteine C-terminal methyltransferase**
CN **Farnesylated protein C-terminal O-methyltransferase**
CN **Farnesylcysteine α-carboxyl methyltransferase**
CN **Gene STE14 methyltransferase**
CN **Geranylgeranylated protein C-terminal methyltransferase**
CN **Geranylgeranylcysteine α-carboxyl methyltransferase**
CN **Isoprenylated protein methyltransferase**
CN **Prenylated protein carboxyl methyltransferase**
CN **Prenylated protein methyltransferase**
CN **Prenylcysteine α-carboxyl methyltransferase**
CN **Prenylcysteine carboxymethyltransferase**
CN **Prenylcysteine-directed carboxyl methyltransferase**
CN **Protein C-terminal farnesylcysteine O-methyltransferase**
CN **Protein S-farnesylcysteine C-terminal methyltransferase**
CN **S-Adenosyl-L-methionine linked-isoprenylated protein methyltransferase**
CN **S-Adenosylmethionine-dependent geranylgeranylated protein methyltransferase**
CN **S-Farnesylcysteine methyltransferase**
MF **Unspecified**
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
84 REFERENCES IN FILE CA (1907 TO DATE)
84 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:297278

REFERENCE 2: 140:268547

REFERENCE 3: 140:214537

REFERENCE 4: 140:178665

REFERENCE 5: 140:88719

REFERENCE 6: 140:35904

REFERENCE 7: 139:271015

REFERENCE 8: 139:115130

REFERENCE 9: 138:333473

REFERENCE 10: 138:315628

L80 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9032-79-5** REGISTRY
CN **Dimethylallyltransferase (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **(2E,6E)-Farnesyl diphosphate synthetase**
CN **Diprenyltransferase**
CN E.C. 2.5.1.1
CN Geranyl diphosphate synthase
CN Geranyl pyrophosphate synthase
CN Geranyl pyrophosphate synthetase
CN Isoprenyl diphosphate synthase
CN **Prenyltransferase**
CN **trans-Farnesyl pyrophosphate-squalene synthetase**
CN **trans-Prenyl transferase**
MF **Unspecified**
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CIN, EMBASE, NAPRALERT, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: PREP (Preparation)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
297 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
298 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:333562

REFERENCE 2: 140:299274

REFERENCE 3: 140:234476

REFERENCE 4: 140:159640

REFERENCE 5: 140:107355

REFERENCE 6: 140:106106

REFERENCE 7: 139:380050

REFERENCE 8: 139:346639

REFERENCE 9: 139:79189

REFERENCE 10: 138:281949

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L79 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **146296-41-5** REGISTRY
CN L-Methionine, N-acetyl-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-(N-acetyl-L-cysteinyl)-L-valyl]-L-isoleucyl]-
OTHER NAMES:
CN PN: US5976851 FIGURE: 13 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **4**
NTE modified

| type | location | description |
|---|---|---|
| terminal mod. | Cys-1 - | N-acetyl |

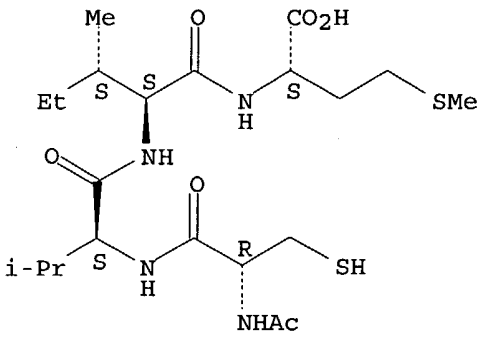
PATENT ANNOTATIONS (PNTE):

| Sequence Source | Patent Reference |
|---|---|
| Not Given | US5976851 claimed FIGURE 13 |

SEQ 1 CVIM
====
HITS AT: 1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF C21 H38 N4 O6 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study)
RLD.NP Roles for non-specific derivatives from non-patents: PROC (Process); PRP (Properties)

Absolute stereochemistry.




8 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:364653

REFERENCE 2: 138:250721

REFERENCE 3: 138:250719

REFERENCE 4: 132:148502

REFERENCE 5: 131:319666

REFERENCE 6: 131:141241

REFERENCE 7: 121:53129

REFERENCE 8: 118:119560

L79 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **139553-04-1** REGISTRY
CN L-Methionine, S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-[S-(3,7,11-trimethyl-2,6,10-dodecatrienyl)-L-cysteinyl]-L-valyl]-L-isoleucyl]-, (E,E)-
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **4**
NTE modified (modifications unspecified)

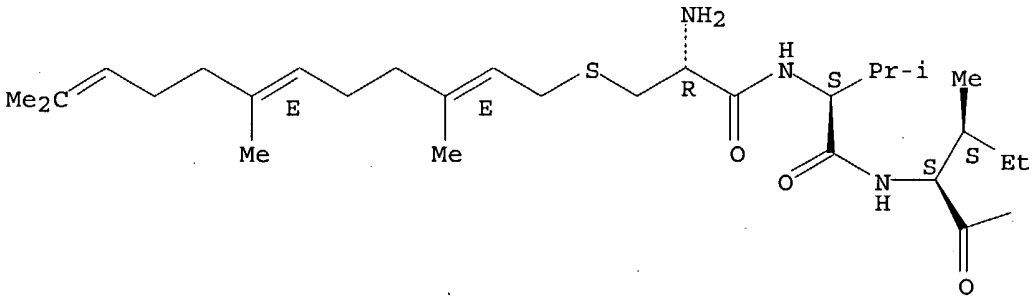
| type | ------ location ------ | | description |
|---|---|---|---|
| modification | Cys-1 | - | undetermined modification |

SEQ 1 CVIM
==== 
HITS AT: 1-4

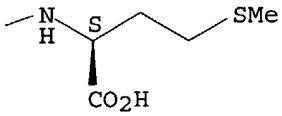
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF C34 H60 N4 O5 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:108298

REFERENCE 2: 116:120882

L79 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **138166-32-2** REGISTRY
CN L-Methionine, N-octyl-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-(N-octyl-L-cysteinyl)-L-valyl]-L-isoleucyl]-
OTHER NAMES:
CN PN: US5976851 FIGURE: 13 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **4**
NTE modified (modifications unspecified)

| type | ------ location ------ | description |
|---|---|---|
| modification | Cys-1 - | undetermined modification |

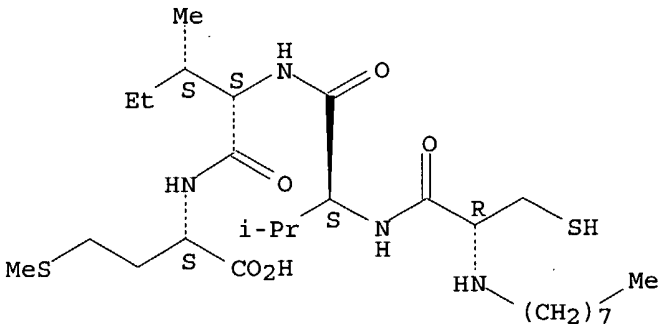
PATENT ANNOTATIONS (PNTE):

| Sequence Source | Patent Reference |
|---|---|
| Not Given | US5976851 claimed FIGURE 13 |

SEQ 1 CVIM
==== 
HITS AT: 1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF C27 H52 N4 O5 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study)
RL.NP Roles from non-patents: RACT (Reactant or reagent)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 116:17650

L79 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **129931-69-7** REGISTRY
CN L-Methionine, L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-(N-L-cysteinyl-L-valyl)-L-isoleucyl]-
OTHER NAMES:
CN 20: PN: WO0025789 SEQID: 1 unclaimed sequence
CN 351: PN: WO03012068 SEQID: 362 claimed sequence
CN PN: US5976851 SEQID: 10 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **4**

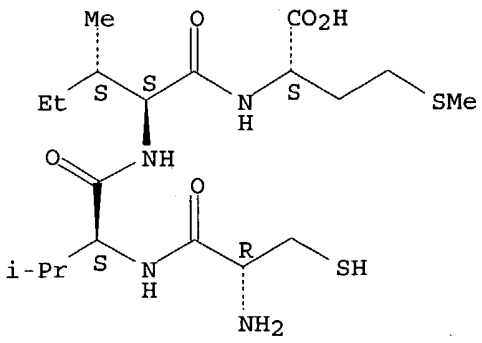
PATENT ANNOTATIONS (PNTE):

| Sequence Source | Patent Reference |
|---|---|
| Not Given | US5976851 claimed SEQID 10 |
| | WO2000025789 unclaimed SEQID 1 |

SEQ 1 CVIM
==== 
HITS AT: 1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF C19 H36 N4 O5 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties); RACT (Reactant or reagent)

Absolute stereochemistry.



21 REFERENCES IN FILE CA (1907 TO DATE)
21 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:164688

REFERENCE 2: 133:116599

REFERENCE 3: 132:343356

REFERENCE 4: 131:319666

REFERENCE 5: 131:254315

REFERENCE 6: 130:218275

REFERENCE 7: 130:206600

REFERENCE 8: 128:110864

REFERENCE 9: 126:207508

REFERENCE 10: 126:28543

L79 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **129931-68-6** REGISTRY
CN L-Methionine, L-threonyl-L-lysyl-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-[N-(N2-L-threonyl-L-lysyl)-L-cysteinyl]-L-valyl]-L-isoleucyl]-
OTHER NAMES:
CN PN: US5976851 SEQID: 9 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **6**

PATENT ANNOTATIONS (PNTE):

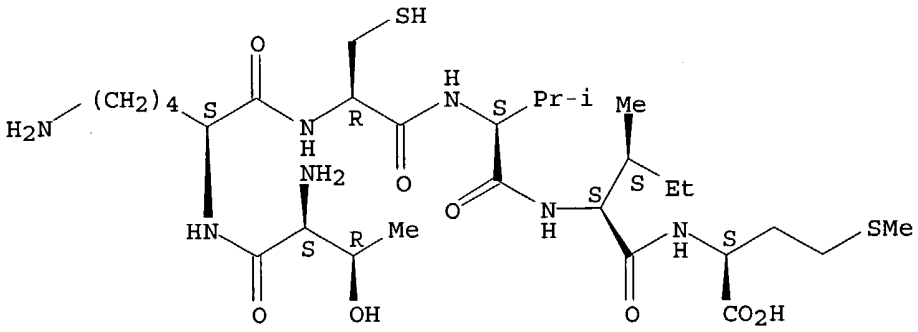
| Sequence Source | Patent Reference |
|---|---|
| Not Given | US5976851 claimed SEQID 9 |

SEQ 1 TKCVIM
======
HITS AT: 1-6

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

MF C29 H55 N7 O8 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties)
RLD.NP Roles for non-specific derivatives from non-patents: PRP (Properties)

Absolute stereochemistry.



10 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:257225

REFERENCE 2: 132:305114

REFERENCE 3: 131:319666

REFERENCE 4: 131:254315

REFERENCE 5: 130:261548

REFERENCE 6: 130:206600

REFERENCE 7: 129:146124

REFERENCE 8: 126:28543

REFERENCE 9: 117:43554

REFERENCE 10: 114:117328

L79 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN **129931-67-5** REGISTRY
CN L-Methionine, L-lysyl-L-lysyl-L-seryl-L-lysyl-L-threonyl-L-lysyl-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Methionine, N-[N-[N-[N-[N2-[N-[N2-[N-(N2-L-lysyl-L-lysyl)-L-seryl]-L-lysyl]-L-threonyl]-L-lysyl]-L-cysteinyl]-L-valyl]-L-isoleucyl]-
OTHER NAMES:
CN PN: US5976851 SEQID: 11 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **10**

PATENT ANNOTATIONS (PNTE):
Sequence |Patent

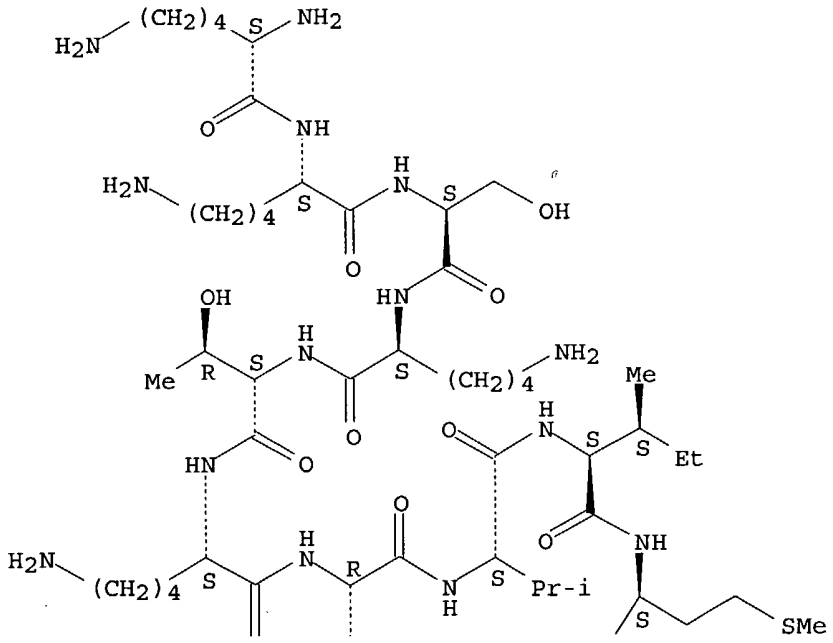
| Source | Reference |
|---|---|
| Not Given | US5976851 |
| | claimed |
| | SEQID 11 |

SEQ 1 KKSKTKCVIM
==========
HITS AT: 1-10

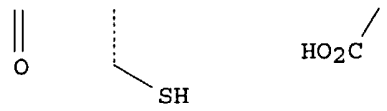
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF C50 H96 N14 O13 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study)
RL.NP Roles from non-patents: BIOL (Biological study)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 117:43554

REFERENCE 5: 114:117328

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L81 ANSWER 1 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **156200-47-4** REGISTRY
CN **Farnesyltransferase, protein (cysteine) (human β-subunit C-terminal fragment reduced) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN PN: US5976851 FIGURE: 24 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:53129

L81 ANSWER 2 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **156200-46-3** REGISTRY
CN **DNA (human protein (cysteine) farnesyltransferase α-subunit cDNA plus 3'-flank) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid (human protein (cysteine) farnesyltransferase α-subunit messenger RNA-complementary plus 3'-flanking region fragment)**
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:254315

REFERENCE 2: 126:28543

REFERENCE 3: 121:53129

L81 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **151210-93-4** REGISTRY
CN **DNA (human protein (cysteine) farnesyltransferase β-subunit C-terminal fragment-specifying plus 3'-flank) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid (human protein (cysteine) farnesyltransferase β-subunit C-terminal fragment-specifying plus 3'-flanking region fragment)**
OTHER NAMES:
CN PN: US5976851 FIGURE: 24 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:53129

REFERENCE 5: 120:262627

L81 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **151210-92-3** REGISTRY
CN **DNA (human retina protein (cysteine) farnesyltransferase α-subunit cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid (human retina protein (cysteine) farnesyltransferase α-subunit messenger RNA-complementary plus 5'- and 3'-flanking region fragment)**
OTHER NAMES:
CN DNA (human clone WO0118542_SEQID_600 ovary tumor-associated protein cDNA)
CN **DNA (human farnesyl-protein transferase α-subunit cDNA)**
CN PN: US5976851 FIGURE: 23 claimed DNA
CN PN: WO0118542 SEQID: 600 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:146104

REFERENCE 2: 134:336654

REFERENCE 3: 134:234030

REFERENCE 4: 131:319666

REFERENCE 5: 120:262627

L81 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **148222-53-1** REGISTRY
CN **Farnesyltransferase, protein (cysteine) (human placenta α-subunit reduced) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **Farnesyl-protein transferase (human placenta α subunit)**
CN PN: US5976851 FIGURE: 23 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:275273

REFERENCE 5: 121:53129

REFERENCE 6: 120:262627

REFERENCE 7: 119:23607

L81 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **146634-75-5** REGISTRY
CN **Farnesyltransferase, protein (cysteine) (rat clone λRTH α-subunit reduced) (9CI)** (CA INDEX NAME)

OTHER NAMES:
CN PN: US5976851 FIGURE: 17 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:53129

REFERENCE 5: 118:164045

L81 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **146634-74-4** REGISTRY
CN **DNA (rat clone λRTH protein (cysteine) farnesyltransferase α-subunit cDNA) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid (rat clone λRTH protein (cysteine) farnesyltransferase α-subunit messenger RNA-complementary)**
OTHER NAMES:
CN PN: US5976851 FIGURE: 17 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 118:164045

L81 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **142298-65-5** REGISTRY
CN **Farnesyltransferase, protein (cysteine) (rat clone λRB-23 β-subunit reduced) (9CI)** (CA INDEX NAME)

OTHER NAMES:
CN PN: US5976851 FIGURE: 18 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:53129

REFERENCE 5: 117:41617

L81 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **142244-36-8** REGISTRY
CN **DNA, (rat clone λRB-23 protein (cysteine) farnesyltransferase β-subunit cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid, (rat clone λRB-23 protein (cysteine) farnesyltransferase β-subunit messenger RNA-complementary plus 5'- and 3'-flanking region fragment)**
OTHER NAMES:
CN PN: US5976851 FIGURE: 18 claimed DNA
FS NUCLEIC ACID SEQUENCE
DR 140085-44-5
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 121:53129

REFERENCE 5: 117:41617

L81 ANSWER 10 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **142244-35-7** REGISTRY
CN **DNA (rat clone λRB-23 protein (cysteine) farnesyltransferase β-subunit cDNA) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid (rat clone λRB-23 protein (cysteine) farnesyltransferase β-subunit messenger RNA-complementary)**
OTHER NAMES:
CN PN: US5976851 FIGURE: 18 claimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

REFERENCE 2: 117:41617

L81 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **140107-18-2** REGISTRY
CN **DNA, (rat clone λRTH protein (cysteine) farnesyltransferase α-subunit cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Deoxyribonucleic acid, (rat clone λRTH protein (cysteine) farnesyltransferase α-subunit messenger RNA-complementary plus 5'- and 3'-flanking region fragment)**
OTHER NAMES:
CN PN: US5976851 FIGURE: 17 claimed DNA
FS NUCLEIC ACID SEQUENCE
DR 145347-38-2
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:319666

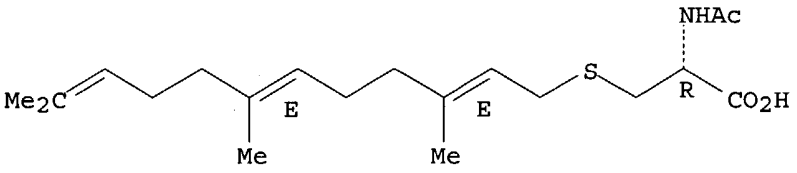
REFERENCE 2: 131:254315

REFERENCE 3: 126:28543

REFERENCE 4: 118:164045

L81 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **135304-07-3** REGISTRY
CN L-Cysteine, N-acetyl-S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Cysteine, N-acetyl-S-(3,7,11-trimethyl-2,6,10-dodecatrienyl)-, (E,E)-
OTHER NAMES:
CN **N-Acetyl-L-farnesylcysteine**
CN **N-Acetyl-S-farnesyl-L-cysteine**
CN **N-Acetyl-S-trans,trans-farnesyl-L-cysteine**
FS STEREOSEARCH
DR 345287-43-6
MF C20 H33 N O3 S
SR CA
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS,
CASREACT, CHEMCATS, CSCHEM, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
(Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
study); PREP (Preparation); PROC (Process); PRP (Properties); RACT
(Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

53 REFERENCES IN FILE CA (1907 TO DATE)
53 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:297278

REFERENCE 2: 139:271014

REFERENCE 3: 138:333473

REFERENCE 4: 137:166818

REFERENCE 5: 137:6035

REFERENCE 6: 136:304101

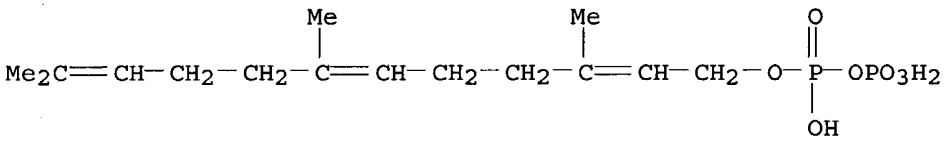
REFERENCE 7: 136:210502

REFERENCE 8: 135:137685

REFERENCE 9: 135:57494

REFERENCE 10: 134:340667

L81 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **13058-04-3** REGISTRY
CN Diphosphoric acid, mono(3,7,11-trimethyl-2,6,10-dodecatrienyl) ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,6,10-Dodecatrien-1-ol, 3,7,11-trimethyl-, trihydrogen pyrophosphate (8CI)
CN **Farnesyl pyrophosphate (6CI)**
OTHER NAMES:
CN Farnesol pyrophosphate
CN **Farnesyl diphosphate**
CN **Farnesyl trihydrogen pyrophosphate**
FS 3D CONCORD
MF C15 H28 O7 P2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

347 REFERENCES IN FILE CA (1907 TO DATE)
19 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
351 REFERENCES IN FILE CAPLUS (1907 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:352650

REFERENCE 2: 140:317117

REFERENCE 3: 140:317025

REFERENCE 4: 140:247122

REFERENCE 5: 140:159986

REFERENCE 6: 140:124512

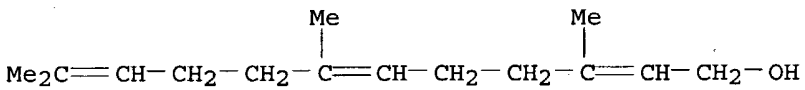
REFERENCE 7: 140:14292

REFERENCE 8: 139:348440

REFERENCE 9: 139:304596

REFERENCE 10: 139:288020

L81 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **4602-84-0** REGISTRY
CN 2,6,10-Dodecatrien-1-ol, 3,7,11-trimethyl- (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Farnesol (6CI)
OTHER NAMES:
CN 3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol
CN **Farnesyl alcohol**
CN FCI 119a
CN Nikkosome
CN NSC 60597
FS 3D CONCORD
MF C15 H26 O
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1676 REFERENCES IN FILE CA (1907 TO DATE)

49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1678 REFERENCES IN FILE CAPLUS (1907 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:326767

REFERENCE 2: 140:326759

REFERENCE 3: 140:326646

REFERENCE 4: 140:320283

REFERENCE 5: 140:320182

REFERENCE 6: 140:318305

REFERENCE 7: 140:316591

REFERENCE 8: 140:308979

REFERENCE 9: 140:297121

REFERENCE 10: 140:292199

L81 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2004 ACS on STN
RN **372-97-4** REGISTRY
CN Diphosphoric acid, mono[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl] ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,6,10-Dodecatrien-1-ol, 3,7,11-trimethyl-, trihydrogen pyrophosphate, (E,E)- (8CI)
CN Diphosphoric acid, mono(3,7,11-trimethyl-2,6,10-dodecatrienyl) ester, (E,E)-
OTHER NAMES:
CN **(2E,6E)-Farnesyl diphosphate**
CN **(2E,6E)-Farnesyl pyrophosphate**
CN **(all-E)-Farnesyl diphosphate**
CN **(E,E)-Farnesyl diphosphate**
CN **(E,E)-Farnesyl pyrophosphate**
CN **2-trans,6-trans-Farnesyl pyrophosphate**
CN **all-trans-Farnesyl pyrophosphate**
CN **Farnesyl pyrophosphate**
CN SQ 32709
CN **trans,trans-Farnesyl diphosphate**
CN **trans,trans-Farnesyl pyrophosphate**
CN **trans-Farnesyl pyrophosphate**
FS STEREOSEARCH
MF C15 H28 O7 P2
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CIN, EMBASE, NIOSHTIC, PHAR, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or

reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

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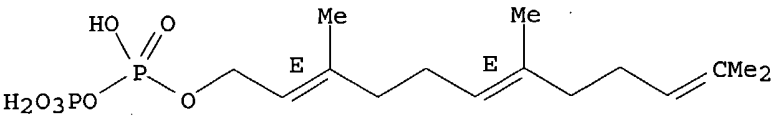


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

294 REFERENCES IN FILE CA (1907 TO DATE)
24 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
294 REFERENCES IN FILE CAPLUS (1907 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:266700

REFERENCE 2: 140:210217

REFERENCE 3: 140:37841

REFERENCE 4: 140:14363

REFERENCE 5: 140:12957

REFERENCE 6: 139:319156

REFERENCE 7: 139:210676

REFERENCE 8: 139:193584

REFERENCE 9: 139:159743

REFERENCE 10: 139:67817

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FILE LAST UPDATED: 24 May 2004 (20040524/ED)

This file contains CAS Registry Numbers for easy and accurate

substance identification.

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L76 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:704917 HCAPLUS
DN 131:319666
ED Entered STN: 04 Nov 1999
TI **Methods** and compositions for the identification, characterization, and **inhibition** of **farnesyl protein transferase**
IN **Brown, Michael S.; Goldstein, Joseph L.; Reiss, Yuval**
PA Board of Regents, the University of Texas System, USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 822.011, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC C12N009-10
NCL 435193000
CC 7-2 (**Enzymes**)
Section cross-reference(s): 3, 63
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5976851 | A | 19991102 | US 1993-21625 | 19930216 <-- |
| | US 5141851 | A | 19920825 | US 1990-615715 | 19901120 <-- |
| | WO 9116340 | A1 | 19911031 | WO 1991-US2650 | 19910418 <-- |
| | W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US | | | | |
| | RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG | | | | |
| | US 5420245 | A | 19950530 | US 1992-863169 | 19920403 <-- |
| | US 5962243 | A | 19991005 | US 1995-429964 | 19950427 <-- |
| PRAI | US 1990-510706 | B2 | 19900418 <-- | | |
| | US 1990-615715 | A2 | 19901120 <-- | | |
| | WO 1991-US2650 | A2 | 19910418 <-- | | |
| | US 1992-822011 | B2 | 19920116 | | |
| | US 1992-937893 | A2 | 19921222 <-- | | |
| | US 1993-21625 | A2 | 19930216 | | |

AB Disclosed are **methods** and compns. for the identification, characterization and **inhibition** of mammalian **farnesyl protein transferases**, enzymes involved in the **farnesylation** of various cellular proteins, including cancer related **ras** proteins such as **p21ras.** The nucleotide and amino acid sequences of the α and β subunits of both rat and human **farnesyl transferase** are disclosed, as are **methods** and compns. for the preparation of **farnesyl transferase** by recombinant means, following the mol. cloning and co-expression of its two subunits, for assay and purification of the enzyme, as well as procedures for using the purified enzyme in **screening** protocols for the identification of possible anticancer agents which **inhibit** the enzyme and thereby **prevent** expression of proteins such as **p21ras.** Also disclosed is a families of compds. which act either as false substrates for the enzyme or as pure **inhibitors** and can therefore be employed for **inhibition** of the enzyme. The most potent **inhibitors** are ones in which phenylalanine occurs at the third position of a tetrapeptide whose amino terminus is cysteine.
ST protein **farnesyltransferase** cDNA sequence human rat; antitumor **screening** protein **farnesyltransferase inhibitor**
IT Rat

(**farnesyl protein transferase** α- and β-subunits from rat and human)

IT **Drug screening**
(for anticancer compds.; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT cDNA sequences
(for **farnesyl protein transferase** α- and β-subunits from rat and human)

IT Molecular cloning
Plasmid vectors
Virus vectors
(**methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT Protein sequences
(of **farnesyl protein transferase** α- and β-subunits from rat and human)

IT **Ras proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**p21Ha-ras**, substrate; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT Antitumor agents
(**screening** for; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 147259-21-0
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(adaptor; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT **142298-65-5 146634-75-5 148222-53-1 156200-47-4**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248909-00-4 248909-01-5 248909-02-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(consensus peptide **inhibitor**; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248909-06-0 248909-07-1
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(consensus peptide; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 133824-26-7 133824-34-7 248252-34-8 248252-35-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(control peptide; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248252-39-3 248252-40-6

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(epitope for antibody production; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 125464-27-9 **129931-67-5 129931-68-6**
**129931-69-7** 129931-70-0 129931-71-1 129931-72-2
129931-73-3 129931-74-4 133824-11-0 133824-12-1 133824-13-2
133824-14-3 133824-15-4 133824-16-5 133824-17-6 133824-18-7
133824-19-8 133824-20-1 133824-21-2 133824-22-3 133824-23-4
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133824-36-9 133824-38-1 133824-39-2 133824-40-5 133824-41-6
133824-42-7 133824-43-8 133838-26-3 133838-27-4 138143-69-8
138143-71-2 138143-74-5 **138166-32-2**, N-Octyl-**CVIM**
**146296-41-5** 248908-99-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT **131384-38-8**, Protein **farnesyltransferase**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 111863-82-2 133824-37-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248252-37-1 248252-38-2 249269-66-7
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT **140107-18-2 142244-35-7**, DNA (rat clone λRB-23 protein (cysteine) **farnesyltransferase** β-subunit cDNA)
**142244-36-8 146634-74-4**, DNA (rat clone λRTH protein (cysteine) **farnesyltransferase** α-subunit cDNA)
**151210-92-3 151210-93-4**
RL: ARU (Analytical role, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 147259-22-1 248909-03-7 248909-04-8 248909-05-9 249269-62-3
249269-63-4 249269-64-5
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(primer; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 249269-65-6
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(probe; **methods** and compns. for the identification,

characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248252-36-0D, biotinylated
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

IT 248252-41-7 248252-42-8 248252-43-9 248252-44-0 248252-45-1
248252-46-2 248252-47-3 248252-48-4 248252-49-5 248252-50-8
248252-51-9
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(tryptic peptide fragment; **methods** and compns. for the identification, characterization, and **inhibition** of **farnesyl protein transferase**)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; EP 0456180 1991 HCAPLUS
(2) Anon; EP 0461869 A2 1991 HCAPLUS
(3) Anon; WO 9116340 1991 HCAPLUS
(4) Anon; EP 0520823 1992 HCAPLUS
(5) Anon; EP 0523873 1993 HCAPLUS
(6) Anon; EP 0528486 1993 HCAPLUS
(7) Anon; EP 0535730 1993 HCAPLUS
(8) Anon; EP 0535731 1993 HCAPLUS
(9) Anon; GB 2261373 1993 HCAPLUS
(10) Anon; GB 2261374 1993 HCAPLUS
(11) Anon; GB 2261375 1993 HCAPLUS
(12) Anon; WO 9403597 1994 HCAPLUS
(13) Anon; WO 9410184 1994 HCAPLUS
(14) Barbacid; US 5185248 1993 HCAPLUS
(15) Bartizal; US 5026554 1991 HCAPLUS
(16) Bartizal; US 5055487 1991 HCAPLUS
(17) Bos; Cancer Research 1989, V49, P4682 HCAPLUS
(18) Casey; Proc Natl Acad Sci 1989, V86, P8323 HCAPLUS
(19) Chen; Cell 1991, V66, P327 HCAPLUS
(20) Clark; US 4675285 1987 HCAPLUS
(21) Clarke; Proc Natl Acad Sci 1988, V85, P4643 HCAPLUS
(22) Goldstein; J Biol Chem 1991, V266(24), P15575 HCAPLUS
(23) Goldstein; Nature 1990, V343, P425 HCAPLUS
(24) Hancock; Cell 1989, V57, P1167 HCAPLUS
(25) Lowy; Nature 1989, V341, P384 MEDLINE
(26) Manne; Proc Natl Acad Sci 1990, V87, P7541 HCAPLUS
(27) Nancy, E; Science 1993, V260, P1934
(28) Rando; US 5202456 1993 HCAPLUS
(29) Reiss; Cell 1990, V62, P81 HCAPLUS
(30) Reiss; Proc Natl Acad Sci 1991, V88, P732 HCAPLUS
(31) Schaber; J Biolog Chem 1990, V265(25), P14701 HCAPLUS
(32) Schafer; Science 1989, V245, P379 HCAPLUS
(33) Singh; US 5245061 1993 HCAPLUS
(34) Stock; US 5043268 1991 HCAPLUS

L76 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:636050 HCAPLUS
DN 131:254315
ED Entered STN: 07 Oct 1999
TI Purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**
IN **Brown, Michael S.**; **Goldstein, Joseph L.**; James, Guy L.
PA Board of Regents, the University of Texas System, USA
SO U.S., 103 pp., Cont.-in-part of U.S. Ser. No. 21,625, abandoned.

CODEN: USXXAM
DT Patent
LA English
IC C12Q001-48; C12N009-10; C07H021-04
NCL 435015000
CC 7-1 (**Enzymes**)
Section cross-reference(s): 1, 3
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | US 5962243 | A | 19991005 | US 1995-429964 | 19950427 | <-- |
| | US 5141851 | A | 19920825 | US 1990-615715 | 19901120 | <-- |
| | WO 9116340 | A1 | 19911031 | WO 1991-US2650 | 19910418 | <-- |
| | W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US | | | | | |
| | RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG | | | | | |
| | US 5420245 | A | 19950530 | US 1992-863169 | 19920403 | <-- |
| | US 5976851 | A | 19991102 | US 1993-21625 | 19930216 | <-- |
| | WO 9634113 | A2 | 19961031 | WO 1996-US5969 | 19960429 | |
| | WO 9634113 | A3 | 19970116 | | | |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | | |
| | AU 9657182 | A1 | 19961118 | AU 1996-57182 | 19960429 | |
| | US 6632626 | B1 | 20031014 | US 2000-665362 | 20000919 | <-- |
| PRAI | US 1990-510706 | B2 | 19900418 | <-- | | |
| | US 1990-615715 | A2 | 19901120 | <-- | | |
| | WO 1991-US2650 | A1 | 19910418 | <-- | | |
| | US 1992-822011 | B2 | 19920116 | | | |
| | US 1992-937893 | A2 | 19921222 | <-- | | |
| | US 1993-21625 | A2 | 19930216 | | | |
| | US 1995-429964 | A | 19950427 | | | |
| | WO 1996-US5969 | W | 19960429 | | | |

AB Disclosed are **methods** and compns. for the identification of **inhibitors** of **farnesyltransferase** (I) enzymes involved in the prenylation of various cellular proteins, including cancer-related **ras** proteins, such as **p21ras** and particularly, K-rasB. Procedures are provided for using purified **farnesyltransferase** enzymes and K-rasB proteins in **screening** protocols for the identification of possible anticancer agents that **inhibit** the enzyme and thereby **prevent** prenylation of proteins such as K-RasB. Thus, I was purified 61,855-fold from rat brains, assayed by transfer of [3H]**farnesol** to **p21H-ras** protein, and a series of tetrapeptides tested for their ability to bind and **inhibit** the enzyme. The recognition site for this enzyme was restricted to 4 amino acids of the Cys-A1-A2-X type, such as the peptide **CVIM** in which **inhibited** I by 50% at a concentration of 0.15 μM. Recombinant cloning allowed sequence determination of the α and β subunit cDNAs for the rat and human enzymes. Specificity of prenylation for K-rasB, H-**Ras** and chimeric H-**Ras** proteins by I as well as **geranylgeranyltransferase**-1 was also studied. In comparison to H-**Ras**, K-rasB exhibits (1) a 50-fold higher affinity for I, an 8-fold decrease in sensitivity to the **farnesyltransferase inhibitor** BZ1-2B, and (3) a susceptibility to high affinity geranylgeranylation by **geranylgeranyltransferase**-1.

ST KrasB peptide **inhibitor farnesyltransferase** antitumor; sequence **farnesyltransferase** cDNA human rat
IT cDNA sequences

(for human and rat protein **farnesyltransferase** α and β subunits and for human gene c-Ki-ras2 protein substrate isoforms)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene rap1B; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Protein sequences
(of human and rat protein **farnesyltransferase** α and β subunits and of human gene c-Ki-ras2 protein substrate isoforms)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(**p21c**-Ki-rasB; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT **Ras proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(**p21c**-Ha-**ras**; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Structure-activity relationship
(protein (cysteine) **farnesyltransferase-inhibiting**; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Antitumor agents
(purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT **142298-65-5P 146634-75-5P 148222-53-1P 156200-47-4P**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 87397-64-6, Protein (human Calu-1 cell gene c-Ki-ras2 exon 4A-containing reduced) 87397-65-7, Protein (human Calu-1 cell gene C-Ki-ras2 exon 4B-containing reduced)
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 125464-27-9 **129931-67-5 129931-68-6**
**129931-69-7** 129931-70-0 129931-71-1 129931-72-2
129931-73-3 129931-74-4 133824-11-0 133824-12-1 133824-13-2
133824-14-3 133824-15-4 133824-16-5 133824-17-6 133824-18-7
133824-19-8 133824-20-1 133824-21-2 133824-22-3 133824-23-4
133824-27-8 133824-28-9 133824-29-0 133824-30-3 133824-31-4
133824-32-5 133824-36-9 133824-37-0 133824-38-1 133824-39-2
133824-40-5 133824-41-6 133838-26-3 133838-27-4 138143-69-8
138143-74-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitory** peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 87396-90-5, DNA (human Calu-1 lung carcinoma gene c-Ki-ras2 exon 4B-containing cDNA) 87396-93-8, DNA (human SW480 colon carcinoma gene c-Ki-ras2 exon 4A-containing cDNA) **140107-18-2** **142244-36-8** **151210-93-4** **156200-46-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT **131384-38-8P**, Protein **farnesyltransferase**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 135371-29-8, Protein **geranylgeranyltransferase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 184637-22-7 184637-23-8 184637-24-9 184637-25-0 184637-26-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(substrate peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 184637-21-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anderegg; JBC 1988, V263, P18236 HCAPLUS
(2) Anon; EP 0456180 1991 HCAPLUS
(3) Anon; EP 0461869 A2 1991 HCAPLUS
(4) Anon; WO 9116340 1991 HCAPLUS
(5) Anon; EP 0520823 1992 HCAPLUS
(6) Anon; EP 0523873 1993 HCAPLUS
(7) Anon; EP 0528486 1993 HCAPLUS
(8) Anon; EP 0535730 1993 HCAPLUS
(9) Anon; EP 0535731 1993 HCAPLUS
(10) Anon; GB 2261373 1993 HCAPLUS
(11) Anon; GB 2261374 1993 HCAPLUS
(12) Anon; GB 2261375 1993 HCAPLUS
(13) Anon; WO 9403597 1994 HCAPLUS
(14) Anon; WO 9404561 1994 HCAPLUS
(15) Anon; WO 9410184 1994 HCAPLUS
(16) Anon; WO 9512572 1995 HCAPLUS
(17) Anon; WO 9621456 1996 HCAPLUS
(18) Anthony; US 5525479 1996 HCAPLUS
(19) Barcacid; US 5185248 1993 HCAPLUS
(20) Bartizal; US 5026554 1991 HCAPLUS
(21) Bartizal; US 5055487 1991 HCAPLUS

(22) Bos; Cancer Research 1989, V49, P4682
(23) Carney; US 5443956 1995 HCAPLUS
(24) Casey; Proc Natl Acad Sci USA 1989, V86, P8323 HCAPLUS
(25) Chen; US 4677069 1987 HCAPLUS
(26) Chen; Cell 1991, V66, P327 HCAPLUS
(27) Clark; Proc Natl Acad Sci USA 1988, V85, P4643
(28) De Solms; US 5326773 1994 HCAPLUS
(29) Deana; US 5352705 1994 HCAPLUS
(30) Goldstein; Nature 1990, V343, P425 HCAPLUS
(31) Graham; US 5238922 1993 HCAPLUS
(32) Graham; US 5340828 1994 HCAPLUS
(33) Hancock; Cell 1989, V57, P1167 HCAPLUS
(34) Lacal; PNAS 1984, V81, P5305 HCAPLUS
(35) Lowy; Nature 1989, V341, P384 MEDLINE
(36) Manne; Proc Natl Acad Sci USA 1990, V87, P7541 HCAPLUS
(37) McCormick; US 5104975 1992 HCAPLUS
(38) McCormick; US 5234849 1993 HCAPLUS
(39) Rando; US 5202456 1993 HCAPLUS
(40) Reiss; Cell 1990, V62, P81 HCAPLUS
(41) Reiss; Proc Natl Acad Sci USA 1991, V88, P732 HCAPLUS
(42) Schaber; J Biolog Chem 1990, V265(25), P14701 HCAPLUS
(43) Schafer; Science 1989, V245, P379 HCAPLUS
(44) Singh; US 5245061 1993 HCAPLUS
(45) Stock; US 5043268 1991 HCAPLUS
(46) Towler; JBC 1987, V262, P1030 HCAPLUS
(47) Towler; PNAS 1986, V83, P2812 HCAPLUS

L76 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:295 HCAPLUS
DN 126:28543
ED Entered STN: 02 Jan 1997
TI Purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**
IN **Brown, Michael S.**; **Goldstein, Joseph L.**; James, Guy L.
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 257 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-48
ICS C07K014-82
CC 7-1 (**Enzymes**)
Section cross-reference(s): 1, 3
FAN.CNT 4

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|---|
| PI | WO 9634113 | A2 | 19961031 | | WO 1996-US5969 | 19960429 | |
| | WO 9634113 | A3 | 19970116 | | | | |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | | | |
| | US 5962243 | A | 19991005 | | US 1995-429964 | 19950427 | <-- |
| | AU 9657182 | A1 | 19961118 | | AU 1996-57182 | 19960429 | |
| PRAI | US 1995-429964 | A | 19950427 | | | | |
| | US 1990-510706 | B2 | 19900418 | <-- | | | |
| | US 1990-615715 | A2 | 19901120 | <-- | | | |
| | WO 1991-US2650 | A1 | 19910418 | <-- | | | |
| | US 1992-822011 | B2 | 19920116 | | | | |
| | US 1992-937893 | A2 | 19921222 | <-- | | | |

US 1993-21625 A2 19930216
WO 1996-US5969 W 19960429

AB Disclosed are **methods** and compns. for the identification of **inhibitors** of **farnesyltransferase** (I) enzymes involved in the prenylation of various cellular proteins, including cancer-related **ras** proteins, such as **p21ras** and particularly, K-rasB. Procedures are provided for using purified **farnesyltransferase** enzymes and K-rasB proteins in **screening** protocols for the identification of possible anticancer agents that **inhibit** the enzyme and thereby **prevent** prenylation of proteins such as K-RasB. Thus, I was purified 61,855-fold from rat brains, assayed by transfer of [3H]**farnesol** to **p21H-ras** protein, and a series of tetrapeptides tested for their ability to bind and **inhibit** the enzyme. The recognition site for this enzyme was restricted to 4 amino acids of the Cys-A1-A2-X type, such as the peptide **CVIM** which **inhibited** I by 50% at a concentration of 0.15 μM. Recombinant cloning allowed sequence determination of the α and β subunit cDNAs for the rat and human enzymes. Specificity of prenylation for K-rasB, H-**Ras** and chimeric H-**Ras** proteins by I as well as **geranylgeranyltransferase**-1 was also studied. In comparison to H-**Ras**, K-rasB exhibits (1) a 50-fold higher affinity for I, an 8-fold decrease in sensitivity to the **farnesyltransferase inhibitor** BZ1-2B, and (3) a susceptibility to high affinity geranylgeranylation by **geranylgeranyltransferase**-1.

ST protein KrasB **farnesyltransferase**; sequence **farnesyltransferase** cDNA human rat; anticancer **inhibitor** peptide **farnesyltransferase**

IT cDNA sequences
(for human and rat protein **farnesyltransferase** α and β subunits and for human gene c-Ki-ras2 protein substrate isoforms)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene rap1B; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Protein sequences
(of human and rat protein **farnesyltransferase** α and β subunits and of human gene c-Ki-ras2 protein substrate isoforms)

IT **Ras proteins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(**p21c-Ha-ras**; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(**p21c**-Ki-rasB; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Structure-activity relationship
(protein (cysteine) **farnesyltransferase-inhibiting**; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT Antitumor agents
(purification and characterization of rat and human

**farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT **142298-65-5P 146634-75-5P 148222-53-1P 156200-47-4P**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 87397-64-6, Protein (human Calu-1 cell gene c-Ki-ras2 exon 4A-containing reduced) 87397-65-7, Protein (human Calu-1 cell gene C-Ki-ras2 exon 4B-containing reduced)
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 125464-27-9 **129931-67-5 129931-68-6 129931-69-7** 129931-70-0 129931-71-1 129931-72-2 129931-73-3 129931-74-4 133824-11-0 133824-12-1 133824-13-2 133824-14-3 133824-15-4 133824-16-5 133824-17-6 133824-18-7 133824-19-8 133824-20-1 133824-21-2 133824-22-3 133824-23-4 133824-27-8 133824-28-9 133824-29-0 133824-30-3 133824-31-4 133824-32-5 133824-36-9 133824-37-0 133824-38-1 133824-39-2 133824-40-5 133824-41-6 133838-26-3 133838-27-4 138143-69-8 138143-74-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitory** peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 87396-90-5, DNA (human Calu-1 lung carcinoma gene c-Ki-ras2 exon 4B-containing cDNA) 87396-93-8, DNA (human SW480 colon carcinoma gene c-Ki-ras2 exon 4A-containing cDNA) **140107-18-2 142244-36-8 151210-93-4 156200-46-3**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT **131384-38-8P**, Protein **farnesyltransferase**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 135371-29-8, Protein **geranylgeranyltransferase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 184637-22-7 184637-23-8 184637-24-9 184637-25-0 184637-26-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(substrate peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

IT 184637-21-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(substrate peptide; purification and characterization of rat and human **farnesyltransferase** enzymes, **methods** for assay of their activity, and identification of **inhibitors**)

L76 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:443554 HCAPLUS
DN 117:43554
ED Entered STN: 08 Aug 1992
TI Preparation, identification, characterization, and **inhibition** of **farnesyl protein transferase**
IN **Brown, Michael S.**; **Goldstein, Joseph L.**; **Reiss, Yuval**
PA University of Texas System, USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K007-06
ICS C12N009-10; C12N015-54; C12Q001-48; C07K005-10; A61K037-02
CC 7-2 (**Enzymes**)
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|
| PI | WO 9116340 | A1 | 19911031 | WO 1991-US2650 | 19910418 | <-- |
| | W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US | | | | | |
| | RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG | | | | | |
| | US 5141851 | A | 19920825 | US 1990-615715 | 19901120 | <-- |
| | CA 2076652 | AA | 19911019 | CA 1991-2076652 | 19910418 | <-- |
| | CA 2076652 | C | 20030610 | | | |
| | AU 9176946 | A1 | 19911111 | AU 1991-76946 | 19910418 | <-- |
| | AU 637497 | B2 | 19930527 | | | |
| | EP 528820 | A1 | 19930303 | EP 1991-907853 | 19910418 | <-- |
| | EP 528820 | B1 | 19961009 | | | |
| | EP 528820 | B2 | 20011219 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | | |
| | JP 05506779 | T2 | 19931007 | JP 1991-507785 | 19910418 | <-- |
| | AT 143973 | E | 19961015 | AT 1991-907853 | 19910418 | <-- |
| | US 5976851 | A | 19991102 | US 1993-21625 | 19930216 | <-- |
| | US 5962243 | A | 19991005 | US 1995-429964 | 19950427 | <-- |
| | US 2003170766 | A1 | 20030911 | US 2002-83894 | 20020227 | <-- |
| PRAI | US 1990-510706 | A2 | 19900418 | <-- | | |
| | US 1990-615715 | A2 | 19901120 | <-- | | |
| | WO 1991-US2650 | A | 19910418 | <-- | | |
| | US 1992-822011 | B2 | 19920116 | | | |
| | US 1992-937893 | A2 | 19921222 | <-- | | |
| | US 1993-21625 | A2 | 19930216 | | | |

AB A **farnesyl transferase** (I) that catalyzes transfer of a **farnesyl** group to a protein, e.g. the oncogenic protein **p21ras**, is purified from rat brain. I is a heterodimer with subunits of 45,000 and 50,000 kDa by SDS-PAGE. Its **farnesyl transferase** activity is **inhibited** by oligopeptides that mimic the tetrapeptide CAAX (C = Cys; A = aliphatic amino acids; X = any amino acids) at the C-terminus of the **p21ras**, e.g. **TKCVIM**, **CVIM**, **KKSKTKCVIM**, etc.. Some of these oligopeptides showed 20-40 fold higher affinity fir the enzyme than **p21ras**,. A strategy for cloning the cDNA encoding the α and β subunits of I was also described. The invention can be used for study of the behavior of **p21ras** that is highly related to the

progression and development of a variety of cancers.
ST **farnesyl transferase ras** protein **inhibitor** identification
IT Neoplasm
(diagnosis of, **farnesyl transferase inhibitors** in relation to)
IT Rat
(**farnesyl transferase** for **P21ras** protein purification from)
IT Biotinylation
(of **farnesyl protein transferase inhibitor** tetrapeptide)
IT Acylation
Alkylation
Esterification
(of **farnesyl protein transferase-inhibiting** tetrapeptides)
IT Amino acids, biological studies
RL: BIOL (Biological study)
(aryl, chloro, **farnesyl transferase inhibitor** tetrapeptide containing)
IT Amino acids, biological studies
RL: BIOL (Biological study)
(aryl, fluoro, **farnesyl transferase inhibitor** tetrapeptide containing)
IT Amino acids, biological studies
RL: BIOL (Biological study)
(aryl, nitro, **farnesyl transferase inhibitor** tetrapeptide containing)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(**p21ras**, **farnesyl transferase** for, oligopeptide **inhibitors** for)
IT **13058-04-3**, **Farnesyl** pyrophosphate
RL: BIOL (Biological study)
(**farnesyl** group donor for protein **farnesyl transferase**)
IT 125464-27-9 **129931-67-5 129931-68-6**
**129931-69-7** 129931-70-0 129931-71-1 129931-72-2
129931-73-3 129931-74-4 133824-11-0 133824-12-1 133824-13-2
133824-14-3 133824-15-4 133824-16-5 133824-17-6 133824-18-7
133824-19-8 133824-20-1 133824-21-2 133824-22-3 133824-23-4
133824-27-8 133824-28-9 133824-29-0 133824-30-3 133824-31-4
133824-32-5 133824-36-9 133824-37-0 133824-38-1 133824-39-2
133824-40-5 133824-41-6 133838-26-3 133838-27-4
RL: BIOL (Biological study)
(**farnesyl protein transferase inhibitor**)
IT 52-90-4, Cysteine, biological studies 60-18-4, Tyrosine, biological studies 63-91-2, Phenylalanine, biological studies 73-22-3, Tryptophan, biological studies 7424-00-2
RL: BIOL (Biological study)
(**farnesyl protein transferase inhibitor** tetrapeptide containing)
IT **131384-38-8P**
RL: PREP (Preparation)
(preparation and **inhibition** and characterization of)

L76 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:168954 HCAPLUS
DN 116:168954
ED Entered STN: 03 May 1992
TI **Farnesyl-protein transferase** assay for

compounds that block neoplastic transformation
IN Barbacid, Mariano; Manne, Veeraswamy
PA E. R. Squibb and Sons, Inc., USA
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N009-10
ICS C12Q001-48
CC 7-1 (**Enzymes**)
Section cross-reference(s): 1
FAN.CNT 1

| | PATENT NO. | KIND | DATE | | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|---|---|
| PI | EP 456180 | A1 | 19911113 | | EP 1991-107390 | 19910507 | <-- |
| | EP 456180 | B1 | 19980304 | | | | |
| | R: DE, FR, GB, IT | | | | | | |
| | US 5185248 | A | 19930209 | | US 1990-520570 | 19900508 | <-- |
| | CA 2040529 | AA | 19911109 | | CA 1991-2040529 | 19910416 | <-- |
| | JP 04228099 | A2 | 19920818 | | JP 1991-102633 | 19910508 | <-- |
| | JP 3280042 | B2 | 20020430 | | | | |
| | JP 2002159300 | A2 | 20020604 | | JP 2001-342998 | 19910508 | <-- |
| PRAI | US 1990-520570 | A | 19900508 | <-- | | | |
| | JP 1991-102633 | A3 | 19910508 | | | | |

AB An assay for **farnesyl-protein transferase** activity uses a peptide substrate with the CAAX motif and **farnesyl** pyrophosphate to assay the putative **transferase.** This assay can be used to identify compds. that block neoplastic transformation. Various **ras** proteins were partially purified from recombinant bacteria and incubated with radiolabeled **farnesyl** pyrophosphate and crude **transferase** isolated from porcine kidney. Activity was determined by SDS-PAGE followed by autoradiog. or by a filter binding assay. Purification of the **farnesyl-protein transferase** and optimization of the reaction conditions were described.
ST **farnesyl protein transferase** assay; neoplasm **inhibitor ras** protein **farnesylation**
IT Peptides, uses
RL: USES (Uses)
(CAAX motif-containing, **farnesyl-protein transferase** assay containing, screening for neoplasm **inhibitors** in relation to.)
IT Proteins, specific or class
RL: ANST (Analytical study)
(CAAX motif-containing, **farnesyl-protein transferase** assay substrate, screening for neoplasm **inhibitors** in relation to.)
IT Neoplasm **inhibitors**
(**farnesyl-protein transferase** **inhibitors** as, assay for identification of)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: ANST (Analytical study)
(**gene ras, farnesyl-protein transferase** assay using, screening for neoplasm **inhibitors** in relation to)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: ANST (Analytical study)
(**p21c-Ha-ras, farnesyl-protein transferase** assay using, screening for neoplasm **inhibitors** in relation to.)
IT Gene, animal
RL: ANST (Analytical study)
(c-Ki-**ras**, neoplastic transformation by, **inhibitors** of, assay for identification of)

IT Gene, animal
RL: ANST (Analytical study)
(c-Ha-**ras**, neoplastic transformation by, **inhibitors** of, assay for identification of)
IT Gene, animal
RL: ANST (Analytical study)
(c-**ras**, neoplastic transformation by, **inhibitors** of, assay for identification of)
IT **131384-38-8P**
RL: PREP (Preparation)
(assay for and purification from porcine kidney of, screening for neoplasm **inhibitors** in relation to)
IT **372-97-4**, **Farnesyl** pyrophosphate
RL: ANST (Analytical study)
(**farnesyl-protein transferase** assay using, screening for neoplasm **inhibitors** in relation to)
IT **372-97-4D**, **Farnesyl** pyrophosphate, labeled with tritium
RL: ANST (Analytical study)
(**farnesyl-protein transferase** assay using, screening for neoplasm **inhibitors** in relation to.)

L76 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:120882 HCAPLUS
DN 116:120882
ED Entered STN: 03 Apr 1992
TI **Ras** protein **farnesylation inhibitors** for chemotherapeutic agents
IN Gibbs, Jackson B.; Dixon, Richard A. F.; Garsky, Victor M.; Schraber, Michael D.
PA Merck and Co., Inc., USA
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K037-02
ICS C07K005-10; C07K015-00
CC 1-6 (Pharmacology)
Section cross-reference(s): **7**
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 461869 | A2 | 19911218 | EP 1991-305283 | 19910612 <-- |
| | EP 461869 | A3 | 19920708 | | |
| | R: CH, DE, FR, GB, IT, LI, NL | | | | |
| | CA 2044333 | AA | 19911213 | CA 1991-2044333 | 19910611 <-- |
| | JP 04243893 | A2 | 19920831 | JP 1991-140295 | 19910612 <-- |
| PRAI | US 1990-536840 | | 19900612 <-- | | |
| | US 1991-700232 | | 19910517 | | |

OS MARPAT 116:120882
AB Compds., **methods**, and compns. for **inhibition** of **farnesylation** of the **Ras** protein are provided. The compds. **inhibit** plasma membrane **Ras** protein localization and **prevent** transformation of normal cells into cancer cells. The compds. are peptides or **farnesyl** derivs. thereof and **inhibit farnesyl-protein transferase.** Engineered **RAS** gene products of Saccharomyces cerevisiae were used to study **farnesylation** of **Ras** protein in vitro. Properties of bovine brain **farnesyl -protein transferase** activity are reported.
ST **Ras** protein **farnesylation inhibitor** antitumor; neoplasm **inhibitor Ras farnesylation inhibitor**; peptide **Ras farnesylation inhibitor**; **farnesyl**

**protein transferase inhibitor**
IT Neoplasm **inhibitors**
(**Ras** protein **farnesylation inhibitors**)
IT Cell membrane
(**Ras** protein localization in, **inhibitors** of, for antitumor chemotherapeutic, **Ras** protein **farnesylation inhibition** in relation to)
IT Proteins, specific or class
RL: BIOL (Biological study)
(YPT1, as **farnesylation** substrate for **farnesyl-protein transferase**, **Ras** protein **farnesylation inhibition** in relation to)
IT Therapeutics
(chemo-, **Ras** protein **farnesylation inhibitors**)
IT Alkenylation
(**farnesylation**, of **Ras** protein, **inhibitors** of, for antitumor chemotherapeutic)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(**gene RAS**, engineered, **farnesylation** of, **inhibitors** of)
IT **G proteins (guanine nucleotide-binding proteins)**
RL: BIOL (Biological study)
(**gene ras**, **farnesylation** of, **inhibitors** of, for antitumor chemotherapeutic)
IT G proteins (guanine nucleotide-binding proteins)
RL: BIOL (Biological study)
(gene rho, as **farnesylation** substrate for **farnesyl-protein transferase**, **Ras** protein **farnesylation inhibition** in relation to)
IT 132884-61-8 139573-11-8
RL: PRP (Properties)
(**Ras** protein **farnesylation inhibition** in relation to carboxyl-terminal sequence of)
IT 358-72-5, Dimethylallyl pyrophosphate **372-97-4**, **Farnesyl** pyrophosphate 763-10-0, Geranyl pyrophosphate **4602-84-0**, **Farnesol** 6699-20-3, Geranylgeranyl pyrophosphate 24034-73-9 139553-07-4 139553-08-5 139553-09-6 139573-12-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**Ras** protein **farnesylation inhibitory** activity of)
IT **129931-69-7** 129931-73-3 129931-74-4 139553-03-0 **139553-04-1** 139553-05-2
RL: BIOL (Biological study)
(antitumor chemotherapeutic **inhibitor** of **Ras** protein **farnesylation**)
IT 139553-06-3
RL: BIOL (Biological study)
(carboxyl-terminal sequence of **Ras**-related Rho protein, **Ras** protein **farnesylation inhibition** in relation to)
IT **131384-38-8**
RL: BIOL (Biological study)
(**inhibitors** of, for antitumor chemotherapeutic, **inhibition** of **farnesylation** of **Ras** protein in relation to)

L76 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:530384 HCAPLUS
DN 115:130384
ED Entered STN: 05 Oct 1991

TI S-**Farnesylcysteine methyltransferase** in bovine brain
AU Volker, Craig; Miller, Raymond A.; Stock, Jeffry B.
CS Dep. Chem., Princeton Univ., Princeton, NJ, 08544-1014, USA
SO Methods (San Diego, CA, United States) (**1990**), 1(3), 283-7
CODEN: MTHDE9; ISSN: 1046-2023
DT Journal
LA English
CC 7-1 (**Enzymes**)
AB HPLC assays for C-terminal S-**farnesylcysteine** carboxyl **methyltransferase** activities were developed. The critical feature of these **methods** is the use of the small-mol.-weight substrate N-acetyl-Strans,trans-**farnesyl**-L-cysteine, (AFC), the prepare of which is described. Methylation of AFC (Km value reported) provides a convenient screen for compds. that specifically **inhibit** carboxyl methylation at C-terminal S-**farnesylcysteine** residues. The likely importance of this posttranslational modification to the function of **ras**, nuclear lamin B, and the γ subunit of transducin gives the assays potential import in drug characterization and development.
ST **farnesylcysteine methyltransferase** detn brain **acetylfarnesylcysteine**
IT Brain, composition
(**farnesylcysteine methyltransferase** of, determination of)
IT Michaelis constant
(of **farnesylcysteine methyltransferase**, of brain)
IT **130731-20-3**, S-**Farnesylcysteine methyltransferase**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, of brain, **acetylfarnesylcysteine** as substrate in HPLC assay for)
IT **135304-07-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and use in HPLC assay for brain **farnesylcysteine methyltransferase**)

7/11

9

L76 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:117328 HCAPLUS
DN 114:117328
ED Entered STN: 06 Apr 1991
TI **Inhibition** of purified **p21ras farnesyl: protein transferase** by Cys-AAX tetrapeptides
AU **Reiss, Yuval**; **Goldstein, Joseph L.**; Seabra, Miguel C.; Casey, Patrick J.; **Brown, Michael S.**
CS Univ. Texas Southwest. Med. Cent., Dallas, TX, 75235, USA
SO Cell (Cambridge, MA, United States) (**1990**), 62(1), 81-8
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English
CC 7-2 (**Enzymes**)
AB The identification, purification, and characterization of a **farnesyl: protein transferase** that transfers the **farnesyl** moiety from **farnesyl** pyrophospahte to a cysteine in **p21ras** proteins are reported. The enzyme was purified .apprx.60,000-fold from rat brain cytosol through use of a **chromatog.** step based on the enzyme's ability to bind to a hexapeptide containing the consensus sequence (Cys-AAX) for **farnesylation.** The purified enzyme migrated on gel filtration **chromatog.** with an apparent mol. weight of 70,000-100,000. High resolution SDS-polyacrylamide gels showed 2 closely spaced .apprx.50 kd protein bands in the final preparation The enzyme was **inhibited** competitively by peptides as short as 4 residues that contained the Cys-AAX motif. These peptides acted as alternatively substrates that compacted with **p21H-ras** for **farnesylation.**

Effective peptides included the C-terminal sequences of all known **p21ras** proteins as well as those of lamin A and B.

ST **farnesyl protein transferase** brain cytosol; **p21ras** protein **farnesyl transferase**; peptide specificity **farnesyl transferase** brain

IT Brain, composition
(**farnesyl protein transferase** of cytosol of, purification and characterization and peptide **inhibition** of)

IT Peptides, biological studies
RL: BIOL (Biological study)
(cysteine-containing, **farnesyl protein transferase** of brain cytosol **inhibition** by, cysteine location in relation to)

IT Cytoplasm
(cytosol, **farnesyl protein transferase** of, of brain, purification and characterization and peptides **inhibition** of)

IT Cations
(divalent, **farnesyl protein transferase** of brain cytosol requirement for)

IT **Phospholipoproteins**
RL: BIOL (Biological study)
(**p21c-Ha-ras**, **farnesylation** of, by **farnesyl protein transferase** of brain cytosol)

IT **Lipoproteins**
RL: BIOL (Biological study)
(**p21c-Ki-ras**, **farnesylation** of, by **farnesyl protein transferase** of brain cytosol)

IT Lipoproteins
RL: BIOL (Biological study)
(**p21c**-Ki-rasA, **farnesylation** of, by **farnesyl protein transferase** of brain cytosol)

IT Lipoproteins
RL: BIOL (Biological study)
(**p21c**-Ki-rasB, **farnesylation** of, by **farnesyl protein transferase** of brain cytosol)

IT 111863-82-2 **129931-67-5 129931-68-6**
**129931-69-7** 129931-70-0 129931-71-1 129931-72-2
129931-73-3 129931-74-4
RL: BIOL (Biological study)
(**farnesyl protein transferase** of brain cytosol **inhibition** by, cysteine position in relation to)

IT **131384-38-8P**
RL: PREP (Preparation)
(of brain cytosol, purification and characterization and peptides **inhibition** of)

L76 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:38175 HCAPLUS
DN 114:38175
ED Entered STN: 09 Feb 1991
TI Identification and preliminary characterization of protein-cysteine **farnesyltransferase**
AU Manne, Veeraswamy; Roberts, Daniel; Tobin, Andrew; O'Rourke, Edward; De Virgilio, Marcia; Meyers, Chester; Ahmed, Nasheed; Kurz, Boris; Resh, Marilyn; et al.
CS Dep. Mol. Biol., Squibb Inst. Med. Res., Princeton, NJ, 08543-4000, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1990**), 87(19), 7541-5

CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 7-2 (**Enzymes**)
Section cross-reference(s): 6
AB An enzymic activity(ies) capable of catalyzing the **farnesylation** of unprocessed **Ras p21** proteins in vitro at the correct (Cys-186) residue is described. This **farnesylating** activity is heat-labile, requires Mg2+ or Mn2+, is linear with time and with enzyme concentration, and is present in all mammalian cell lines and tissues tested. Gel filtration anal. of a partially purified preparation of protein **farnesyltransferase** revealed 2 peaks of activity at 250-350 kDa and 80-130 kDa. Availability of an in vitro protein **farnesyltransferase** assay should be useful in screening for potential **inhibitors** of **ras** oncogene function that will not interfere with other aspects of the mevalonate pathway.
ST protein cysteine **farnesyltransferase ras p21**
IT Mammal
(protein-cysteine **farnesyltransferase** identification in)
IT Organ
(protein-cysteine **farnesyltransferase** localization in, of mammal)
IT **Phospholipoproteins**
RL: BIOL (Biological study)
(**p21v-Ha-ras**, **farnesylation** of, by protein-cysteine **farnesyltransferase** of human)
IT **131384-38-8**, Protein-cysteine **farnesyltransferase**
RL: BIOL (Biological study)
(of mammal, isolation and characterization of)
IT 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies
RL: BIOL (Biological study)
(protein-cysteine **farnesyltransferase** of mammal requirement for)

L76 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:38170 HCAPLUS
DN 114:38170
ED Entered STN: 09 Feb 1991
TI Polyisoprenylation of **Ras** in vitro by a **farnesyl-protein transferase**
AU Schaber, Michael D.; O'Hara, Monica B.; Garsky, Victor M.; Mosser, Scott D.; Bergstrom, James D.; Moores, Sheri L.; Marshall, Mark S.; Friedman, Paul A.; Dixon, Richard A. F.; Gibbs, Jackson B.
CS Dep. Mol. Biol., Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SO Journal of Biological Chemistry (**1990**), 265(25), 14701-4
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 7-2 (**Enzymes**)
AB **Farnesylation** of **Ras** occurs in vivo on a Cys residue in the C-terminal sequence-Cys-Val-Leu-Ser (termed a CAAX box). This modification is required for **Ras** membrane localization and cell transforming activity. Using [3H]**farnesyl**-PPi as precursor and Escherichia coli-expressed **Ras**, forms of **Ras** having the CAAX sequence were radiolabeled upon incubation with the cytosolic fraction of bovine brain. Forms of **Ras** having a deletion of the CAAX sequence or a Cys to Ser substitution in this sequence were not substrates. Radioactivity incorporated into **Ras** by bovine brain cytosol was released by treatment with iodomethane but not with methanolic KOH indicating a thioether linkage. HPLC anal. of the cleavage products

on a C-18 column showed a major peak of radioactivity that coeluted with an **farnesol** standard The enzyme responsible for **Ras farnesylation** in bovine brain was .apprx.190 kDa as estimated by gel filtration and required a divalent cation for activity. Nonradioactive **farnesyl**-PPi, geranylgeranyl-PPi, and **Ras** peptides having the C-terminal sequence-Cys-Val-Leu-Ser competed in the assay with IC50 values of 0.7, 1.4, and 1-3 μM, resp. **Farnesol** and **Ras** peptides having the sequence -Ser-Val-Leu-Ser were not **inhibitory.** These results identify a **farnesyl-protein transferase** activity that may be responsible for the polyisoprenylation of **Ras** in intact cells.

ST **farnesyl protein transferase Ras** isoprenylation; **Ras** protein **farnesyl transferase** brain

IT Brain, composition
(**farnesyl protein transferase** cytosol of, **Ras** protein **farnesylation** by)

IT Michaelis constant
(of **farnesyl protein transferase**, of brain cytosol)

IT Cytoplasm
(cytosol, **farnesyl protein transferase** of, of brain, **Ras** protein **farnesylation** by)

IT **Lipoproteins**
RL: BIOL (Biological study)
(**gene ras**, **farnesylation** of, by **farnesyl protein transferase** of brain cytosol)

IT **131384-38-8**
RL: BIOL (Biological study)
(**Ras** protein **farnesylation** by, of brain cytosol)

IT **372-97-4**, **Farnesyl** pyrophosphate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **farnesyl protein transferase** of brain cytosol, kinetics of)

L76 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1967:408102 HCAPLUS
DN 67:8102
ED Entered STN: 12 May 1984
TI The purification of 3,3-dimethylallyl- and geranyl-**transferase** and of isopentenyl pyrophosphate isomerase from pig liver
AU Holloway, Peter W.; Popjak, George
CS 'Shell' Res. Ltd., Sittingbourne, UK
SO Biochemical Journal (**1967**), 104(1), 57-70
CODEN: BIJOAK; ISSN: 0264-6021
DT Journal
LA English
CC 3 (**Enzymes**)
AB The enzyme catalyzing the synthesis of **farnesyl** pyrophosphate from dimethylallyl pyrophosphate and isopentenyl pyrophosphate, or from geranyl pyrophosphate and isopentenyl pyrophosphate, has been purified 100-fold from homogenates of pig liver. The name **prenyltransferase** A is suggested for this enzyme classified at present as **geranyltransferase** (EC 2.5.1.1). The enzyme has an optimum pH of 7.9 and requires Mg2+ as activator in preference to Mn2+; it is **inhibited** by iodoacetamide, N-ethylmaleimide, p-hydroxymercuribenzoate, and phosphate ions in addition to the products of the reaction, inorg. pyrophosphate and **farnesyl** pyrophosphate. From product-**inhibition** studies of the **geranyltransferase** reaction, the order of addition of substrates to and release of products from the enzyme has been deduced; geranyl pyrophosphate combines with the enzyme first, followed by isopentenyl

pyrophosphate. **Farnesyl** pyrophosphate dissociate from the enzyme before inorg. pyrophosphate. The existence of isopentenyl pyrophosphate isomerase in liver is confirmed. **Methods** for the preparation of the pyrophosphate esters of isopentenol, 3,3-dimethylallyl alc., geraniol, and **farnesol** are also described.

ST **PRENYLTRANSFERASE**; ISOPENTENYL PYROPHOSPHATE; **GERANYLTRANSFERASES**; **FARNESYL** PYROPHOSPHATE; PYROPHOSPHATE ISOMERASE; **DIMETHYLALLYLTRANSFERASE**

IT 9033-27-6, Isomerases, isopentenyl pyrophosphate
(preparation and properties of)

IT **9032-79-5**, **Dimethylallyltransferases**
(preparation and properties of, **geranyltransferase** and)

IT 358-72-5P **372-97-4P** 763-10-0P 4898-94-6P 16541-17-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 37277-79-5, **Geranyltransferases**
(separation and properties of, dimethylallyl **transferase** and)

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FILE 'BIOSIS' ENTERED AT 14:46:27 ON 25 MAY 2004


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FROM JANUARY 1969 TO DATE.

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FILE RELOADED: 19 October 2003.

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L109 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN **1992:47434** BIOSIS
DN **PREV199293027409; BA93:27409**
TI PURIFICATION OF RAS **FARNESYL PROTEIN TRANSFERASE.**
AU **REISS Y** [Reprint author]; SEABRA M C; **GOLDSTEIN J L**; **BROWN M S**
CS DEP MOLECULAR GENETICS, UNIVERSITY TEXAS SOUTHWESTERN MEDICAL CENTER DALLAS, 5323 HARRY HINES BOULEVARD, DALLAS, TEX 75235, USA
SO Methods (Orlando), (1990) Vol. 1, No. 3, pp. 241-245.
CODEN: MTHDE9. ISSN: 1046-2023.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 13 Jan 1992
Last Updated on STN: 14 Jan 1992
AB We describe a method for the purification of **farnesyl**: **protein transferase**, an enzyme that transfers a farnesyl group from farnesyl pyrophosphate to a COOH-terminal cysteine in ras proteins, nuclear lamin B, and the γ subunit of bovine transducin. The enzyme is purified to homogeneity from rat brain cytosol through use of an affinity chromatography step based on the enzyme's ability to specifically bind to a hexapeptide containing the consensus sequence for farnesylation. The purification procedure is reproducible and enables the isolation of microgram amounts of purified enzyme from 50 rat brains. Two methods for assaying enzymatic activity are also described. One assay measures the transfer of [3H]farnesyl from [3H]farnesyl pyrophosphate to recombinant H-ras, and the other measures the transfer of [3H]farnesyl to a biotinylated peptide containing the Cys-AAX COOH-terminal sequence of K-rasB.

CC Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - Chemical and physical 10806
Enzymes - Physiological studies 10808
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics)
IT Miscellaneous Descriptors
BOVINE RAT TRANSDUCIN NUCLEAR LAMIN B ENZYME ACTIVITY
ORGN Classifier
Bovidae 85715
Super Taxa
Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 9047-61-4 (TRANSFERASE)

L109 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN **1991:64361** BIOSIS
DN **PREV199140029716; BR40:29716**
TI **FARNESYL PROTEIN TRANSFERASE** AN ENZYME THAT ATTACHES A FARNESYL GROUP TO P21R-A-S PROTEINS.
AU **REISS Y** [Reprint author]; SEABRA M C; **GOLDSTEIN J L**; **BROWN M S**
CS DEP MOLECULAR GENETICS, UNIV TEX SOUTHWESTERN MED CENT, DALLAS, TEX 75235, USA
SO Journal of Cell Biology, (1990) Vol. 111, No. 5 PART 2, pp. 260A.
Meeting Info.: THIRTIETH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, SAN DIEGO, CALIFORNIA, USA, DECEMBER 9-13, 1990. J CELL BIOL.
CODEN: JCLBA3. ISSN: 0021-9525.
DT Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 19 Jan 1991
Last Updated on STN: 19 Jan 1991
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biophysics - Molecular properties and macromolecules 10506
Enzymes - Methods 10804
Enzymes - Chemical and physical 10806
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics)
IT Miscellaneous Descriptors
ABSTRACT
RN 9047-61-4 (TRANSFERASE)

L109 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN **1990:423574** BIOSIS
DN **PREV199090084375; BA90:84375**
TI INHIBITION OF PURIFIED P21R-A-S **FARNESYL PROTEIN TRANSFERASE** BY CYS-AAX TETRAPEPTIDES.
AU **REISS Y** [Reprint author]; **GOLDSTEIN J L**; SEABRA M C; CASEY P J; **BROWN M S**
CS DEP MOLECULAR GENETICS, UNIVERSITY TEXAS SOUTHWESTERN MEDICAL CENTER, DALLAS, TEX 75235, USA
SO Cell, (1990) Vol. 62, No. 1, pp. 81-88.

CODEN: CELLB5. ISSN: 0092-8674.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 22 Sep 1990
Last Updated on STN: 22 Sep 1990
AB We report the identification, purification, and characterization of a **farnesyl:protein transferase** that transfers the farnesyl moiety from farnesyl pyrophosphate to a cysteine in p21ras proteins. The enzyme was purified .apprx. 60,000-fold from rat brain cytosol through use of a chromatography step based on the enzyme's ability to bind to a hexapeptide containing the consensus sequence (Cys-AAX) for farnesylation. The purified enzyme migrated on gel filtration chromatography with an apparent molecular weight of 70,000-100,000. High resolution SDS-polyacrylamide gels showed two closely spaced .apprx. 50 kd protein bands in the final preparation. The enzyme was inhibited competitively by peptides as short as 4 residues that contained the Cys-AAX motif. These peptides acted as alternative substrates that competed with p21H-ras for farnesylation. Effective peptides included the COOH-terminal sequences of all known p21ras proteins as well as those of lamin A and B.
CC Microscopy - Cytology and cytochemistry 01054
Cytology - Animal 02506
Genetics - Animal 03506
Biochemistry methods - Proteins, peptides and amino acids 10054
Biochemistry studies - Proteins, peptides and amino acids 10064
Biophysics - Molecular properties and macromolecules 10506
Enzymes - Methods 10804
Enzymes - Chemical and physical 10806
Enzymes - Physiological studies 10808
Metabolism - Proteins, peptides and amino acids 13012
Nervous system - Physiology and biochemistry 20504
Neoplasms - Biochemistry 24006
Neoplasms - Carcinogens and carcinogenesis 24007
In vitro cellular and subcellular studies 32600
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Genetics; Metabolism; Nervous System (Neural Coordination); Tumor Biology
IT Miscellaneous Descriptors
RAT BRAIN MOLECULAR SEQUENCE DATA AMINO ACID SEQUENCE PEPTIDE SEQUENCE RAS PROTO-ONCOGENES
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 9047-61-4 (TRANSFERASE)

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FILE 'WPIX' ENTERED AT 15:18:37 ON 25 MAY 2004


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=> d l136 all abeq tech abex tot

L136 ANSWER 1 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1996-497642 [49] WPIX
CR 1991-339750 [46]; 1994-083105 [10]; 1995-206308 [27]
DNC C1996-155624
TI Assay for **farnesyl transferase** activity - by determining ability to transfer **farnesyl** moiety to K-Ras B protein, partic. useful for identifying inhibitors.
DC B04 D16
IN **BROWN, M S**; **GOLDSTEIN, J L**; JAMES, G L; **REISS, Y**
PA (TEXA) UNIV TEXAS SYSTEM
CYC 70
PI WO 9634113 A2 19961031 (199649)* EN 257 C12Q001-48 <--
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9657182 A 19961118 (199710) C12Q001-48 <--
WO 9634113 A3 19970116 (199715) C12Q001-48 <--
US 5962243 A 19991005 (199948) C12Q001-48 <--
US 5976851 A 19991102 (199953)# C12N009-10 <--
ADT WO 9634113 A2 WO 1996-US5969 19960429; AU 9657182 A AU 1996-57182 19960429; WO 9634113 A3 WO 1996-US5969 19960429; US 5962243 A **CIP of US 1990-510706 19900418, CIP of US 1990-615715 19901120, CIP of WO 1991-US2650 19910418, Cont of WO 1991-US2650 19910418**, CIP of US 1992-822011 19920116, **CIP of US 1992-937893 19921222**, CIP of US 1993-21625 19930216, US 1995-429964 19950427; US 5976851 A **CIP of US 1990-510706 19900418, CIP of US 1990-615715 19901120, CIP of WO 1991-US2650 19910418**, CIP of US 1992-822011 19920116, US 1993-21625 19930216
FDT AU 9657182 A Based on WO 9634113; US 5962243 A CIP of US 5141851; US 5976851 A CIP of US 5141851
PRAI US 1995-429964 19950427; **US 1990-510706**

**19900418; US 1990-615715 19901120;**
**WO 1991-US2650 19910418;** US 1992-822011
19920116; **US 1992-937893 19921222;** US
1993-21625 19930216
REP 2.Jnl.Ref; WO 9404561; WO 9512572; WO 9621456
IC ICM **C12N009-10; C12Q001-48**
ICS C07H021-04; C07K014-82
AB WO 9634113 A UPAB: 20020128
The following methods are claimed: (1) assaying for the presence of **farnesyl transferase** (FT) activity in an enzyme compsn., comprising determining the ability of the enzyme compsn. to catalyse the transfer of a **farnesyl** moiety to a K-RasB protein, or peptide substrate; and (2) identifying a candidate substance that inhibits a FT enzyme, comprising determining the ability of the candidate substance to inhibit the transfer of a **farnesyl** moiety to a K-RasB protein, or peptide substrate catalysed by a FT enzyme compsn.. Also claimed are: (A) K-RasB protein or peptide for use in a method of: (a) assaying for the presence of FT activity in an enzyme compsn.; or (b) identifying a candidate substance that inhibits a FT enzyme; and (B) assay kit comprising a K-RasB protein or peptide substrate, a standard amount of a FT enzyme compsn., a **farnesyl** pyrophosphate cpd. having a labelled **farnesyl** moiety and opt. a standard amount of a known FT inhibitor.
USE - The prods. and methods are partic. used to identify cpds. that have the ability to reduce, or inhibit FT activity. The use of such inhibitors to block the attachment of prenyl gps. to ras proteins in malignant cells of patients suffering from cancer or precancerous states, will serve to treat or palliate the cancer.
Dwg.0/31
FS CPI
FA AB; DCN
MC CPI: B04-C01; B04-N04; B11-C08E; **B12-K04; D05-H09**

L136 ANSWER 2 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1995-206308 [27] WPIX
CR 1991-339750 [46]; 1994-083105 [10]; 1996-497642 [49]
DNC C1995-095675
TI New **farnesyl transferase** inhibitor peptide(s) - based on **farnesyl** acceptor substrate carboxy terminal sequences, used for the treatment of cancer.
DC B04
IN **BROWN, M S; GOLDSTEIN, J L; REISS, Y**
PA (TEXA) UNIV TEXAS
CYC 1
PI US 5420245 A 19950530 (199527)* 55 A61K037-00
ADT US 5420245 A **CIP of US 1990-510706 19900418, CIP of US 1990-615715 19901120**, Div ex US 1992-822011 19920116, US 1992-863169 19920403
FDT US 5420245 A CIP of US 5141851
PRAI US 1992-822011 19920116; **US 1990-510706 19900418; US 1990-615715 19901120;** US 1992-863169 19920403
IC A61K037-02; C07K005-00; C07K007-00
ICM A61K037-00
ICS A61K037-02; C07K005-00; C07K007-00
AB US 5420245 A UPAB: 20020128
A **farnesyl transferase** (FT) inhibitor peptide is claimed which has 4-10 amino acids and a carboxy terminal sequence -CA'A'X each A' = any aliphatic, aromatic or hydroxy amino acid; X = an amino acid, M,S,Q,C,S,A,L,F,V,P or I
USE - The peptides are used for treating cancers, partic. ras-related cancers.
ADVANTAGE - The peptides can act as false substrates that serve to inhibit the **farnesylation** of natural substrates such as p21ras

or as direct inhibitors which are not themselves **farnesylated.** They are potent inhibitors with IC50 values of 0.01-10 mu M. Dwg.0/22

FS CPI
FA AB; GI; DCN
MC CPI: B04-C01A; B04-C01B; B04-N04A; B14-D06; B14-H01

L136 ANSWER 3 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1995-006660 [01] WPIX
DNC C1995-002313
TI Benzodiazepinones as **farnesyl protein transferase** inhibitors - prevent ras-protein switching, use in cancers, proliferative skin diseases, and to combat fungal infections..
DC B02 C02
IN **BROWN, M S**; CROWLEY, C W; **GOLDSTEIN, J L**; JAMES, G L; MARSTERS, J C; MCDOWELL, R S; OARE, D; RAWSON, T E; REYNOLDS, M; SOMERS, T G; SOMERS, T C
PA (GETH) GENENTECH INC; (TEXA) UNIV TEXAS SYSTEM; (TEXA) UNIV TEXAS
CYC 54
PI WO 9426723 A2 19941124 (199501)* EN 482 C07D243-14
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR BY CA CN CZ FI GE HU JP KG KP KR KZ LK LV MD MG MN MW NO NZ PL RO RU SD SI SK TJ TT UA US UZ VN
AU 9469091 A 19941212 (199521) C07D243-14
WO 9426723 A3 19950202 (199611) C07D243-14
EP 698015 A1 19960228 (199613) EN C07D243-14
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5532359 A 19960702 (199632) 193 A61K031-55
JP 09500615 W 19970121 (199713) 536 C07D243-14
EP 763537 A2 19970319 (199716) EN 341 C07D487-04
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 763537 A3 19971022 (199814) C07D243-14
US 5843941 A 19981201 (199904) A61K031-55
ADT WO 9426723 A2 WO 1994-US5157 19940510; AU 9469091 A AU 1994-69091 19940510; WO 9426723 A3 WO 1994-US5157 19940510; EP 698015 A1 EP 1994-917338 19940510, WO 1994-US5157 19940510; US 5532359 A CIP of US 1993-61961 19930514, Cont of US 1993-82202 19930624, US 1994-328595 19941025; JP 09500615 W JP 1994-525630 19940510, WO 1994-US5157 19940510; EP 763537 A2 Div ex EP 1994-917338 19940510, EP 1996-118160 19940510; EP 763537 A3 Div ex EP 1994-917338 19940510, EP 1996-118160 19940510; US 5843941 A CIP of US 1993-61961 19930514, CIP of US 1993-82202 19930624, WO 1994-US5157 19940510, US 1994-313068 19940926
FDT AU 9469091 A Based on WO 9426723; EP 698015 A1 Based on WO 9426723; JP 09500615 W Based on WO 9426723; EP 763537 A3 Div ex EP 698015; US 5843941 A Based on WO 9426723
PRAI US 1993-82202 19930624; US 1993-61961 19930514;
US 1994-328595 19941025; US 1994-313068 19940926
REP 1.Jnl.Ref; EP 166357; EP 167919; EP 284256; EP 322779; EP 461869; EP 520823; WO 9201683; WO 9404561; 3.Jnl.Ref; DE 2237592; DE 2321705; DE 2540522; US 3927016; US 4280957
IC ICM A61K031-55; C07D243-14; C07D487-04
ICS A61K031-41; A61K031-42; A61K031-425; C07D223-16; C07D223-18; C07D243-10; C07D243-24; C07D401-06; C07D401-14; C07D403-04; C07D403-06; C07D403-10; C07D403-12; C07D403-14; C07D405-06; C07D409-06; C07D409-14; C07D417-12; C07D417-14; C07D498-04; C07D513-04
AB WO 9426723 A UPAB: 19950110
5-Phenyl- or 5-trifluoromethyl- benzodiazepinones of formula (II) and their salts are new. R1 = CF3 or phenyl (substd by R and R'); R, R' = H, halo, 1-6C alkyl, haloalkyl, hydroxyalkyl, or alkoxy, OH, 2-7C alkylcarbonyl, etc.; R4, R44 = H, halo, 1-6C alkyl or haloalkyl, phenyl etc.; R7 = H, halo, or 1-6C alkyl or haloalkyl; W = CONR77R8, CH2CONR77R8, COOR8, etc.; R77 = H, 1-8C alkyl, 2-8C alkenyl or alkynyl,

etc.; R8 = 1-8C alkyl, 2-8C alkenyl or alkynyl, etc.; X = NR24COR25, NR24COR8, etc.; R24 = H, benzyl, halobenzyl, or 1-6C alkyl or haloalkyl; R25 = 1-6C alkyl or alkylamino, 2-6C alkenyl etc.

USE - (II) inhibit **farnesyl protein transferase** and farnesylation of the ras-protein and related low m wt G-proteins. They are used in neoplastic and proliferative diseases, including colorectal carcinoma, exocrine pancreatic carcinoma, and myeloid leukaemias; skin proliferative diseases including psoriasis, lichen planus, verrucas, and seborrhoeic keratosis; also for neurofibromatosis, rheumatoid arthritis, papilloma infection, Kaposi sarcoma, and scleroderma. (II) also inhibit isoprenylation of proteins in microorganisms, notably yeasts and fungi, and are of use in treating fungal infections in plants and animals, including humans, esp for immunocompromised individuals. Examples of plant diseases are blights, rusts and mildews, esp Fusarium wilt. Either plants or soil can be treated. Finally (II) are useful as metal ion and metalloprotein chelators.

ADVANTAGE - (II) are non-peptidyl as many prior art cpds and not subject to their disadvantages, including susceptability to hydrolysis and oxidn, or poor transportation across cell membranes.

Dwg.0/8

FS CPI

FA AB; GI; DCN

MC CPI: B06-D07; B14-A04; B14-C09B; B14-D06; B14-H01; B14-N17; C06-D07; C14-A04; C14-A06; C14-C09B; C14-D06; C14-H01; C14-N17

ABEQ US 5532359 A UPAB: 19960819

A compound represented by structural formula (II):

where R and R'= H, halo(F, Cl, Br, I), C1-C6 alkyl, halo(F, Cl, Br, I)C1-C6 alkyl, C1-C6 alkoxy, hydroxy, hydroxy-C1-C6 alkyl, C1-C6 alkylcarbonyl, and C1-C6 alkyloxycarbonyl; R1 and R2 = H, C1-C6 alkyl, halo(F, Cl, Br, I)-C1-C6 alkyl, and (i); R1+R2 = a covalent bond or fused benzene substituted with R and R'; R4 and R4' = H, halo(F, Cl, Br, I), C1-C6 alkyl, halo(F, Cl, Br, I)C1-C6 alkyl, phenyl, and benzyl; R7 = H, halo(F, Cl, Br, I), C1-C6 alkyl, and halo(F, Cl, Br, I)C1-C6alkyl; W = C(=O)-NR7'R8, CH2-C(=O)-NR7'R8, CR8'(OH)-CHR7R8, CHR8'-CHR7R8, CHR8'-CHR7R8, CR8'CR7R8 (E or Z), C(=O)-CHR7R8, CHR8'-NR7'R8, CHR8'-O-R8, CHR8'-S(O)u-R8 where u is 0, 1, or 2, CR8'=N-R8, CHR8'-R8, W', C1-C3alkyl-W', C6-C12aryl-W', C6-C12aryl-C1-C3alkyl-W', heterocycle-W', heterocycle-C1-C3alkyl-W', C1-C2alkyl-C6-C10aryl-W', and C1-C2alkyl-heterocycle-W', where any heterocycle is a 5- or 6-member saturated or unsaturated ring containing 1 to 3 heteroatoms selected from O, N, and S; W' = H, SR9, SSR9, SC(=O)-R9, OR9, C(=NH)-NH2, N=CH-NH2, NH-CH=NH, R8, and V; R7'= H, benzyl, C1-C4alkyl, and halo(F, Cl, Br, I)C1-C4alkyl; R8' = H, C1-C4alkyl, and halo(F, Cl, Br, I)C1-C4alkyl; NR7'+R8 = pyrrolidinyl or piperidyl ring optionally substituted with one or two groups selected from SR9, SSR9, SC(=O)-R9, OR9, C(=O)NHOH, NHR9, C(=O)NR27R28, and V; R8 opt. substituted C1-C8alkyl, C1-C4alkyl-Z-C1-C4alkyl, where Z is S or O, C2-C4alkyl-NR-C2-C4alkyl, C2-C8alkenyl, C6-C12arylC1-C3alkyl, indol-3-yl-C1-C3alkyl, and imidazol-4-yl-C1-C3alkyl, where any aryl moiety is optionally substituted with -OR9 and V, and where any alkyl or alkenyl group is optionally substituted with one to three groups selected from SR9, SSR9, SC(=O)-R9, OR9, C(=NH)-NH2, N=CH-NH2,

NH-CH=NH, NH-C(=NH)-NH2, C(=O)NHOH, NHR9, C(=O)NR27R28, and V; V = COR10, SO3R13, NHSO2CF3, PO(OR13)2, SO2NHR10, CONHOR13, C(OH)R10PO(OR13)2, CN, SO2NH-heteroaryl where the heteroaryl is a 5- or 6-member aromatic ring containing 1 to 3 heteroatoms selected from O, N, and S and where the heteroaryl is unsubstituted or substituted with one or two substituents selected from the group OH, SH, C1-C4alkyl, C1-C4alkoxy, CF3, halo(F, Cl, Br, I), NO2, COOH, COO-(C1-C4alkyl), NH2, NH(C1-C4alkyl), and N(C1-C4alkyl)2, CONHSO2R15, SO2NHCOR15, CONHSO2R13, CH2CONHSO2R15, NHCONHSO2R15, NHSO2NHCOR15, CONHNHSO2CF3, CON(OH)R13, CONHCOCF3, CONHSO2R10, CONHSO2R11,

CONHSO2R13, (ii) - (vi); R9 = H, methyl, ethyl, isopropyl, phenyl,

and benzyl; R10 = hydroxy, C1-C8-alkoxy, C3-C12-alkenoxy, C6-C12-aryloxy, C1-C6-alkyl-C6-C12-aryloxy, di-C1-C8-alkylamino-C1-C8-alkoxy, alkanoylamino-C1-C8-alkoxy selected from the group acetylaminoethoxy, nicotinoylaminoethoxy, and succinamidoethoxy, and C1-C8-alkanoyloxy-C1-C8-alkoxy, C6-C12-aryl-C1-C8-alkoxy where the aryl group is opt. substituted with 1-3 of nitro, halo(F, Cl, Br, I), C1-C4-alkoxy, and amino, hydroxy-C2-C8-alkoxy, dihydroxy-C3-C8-alkoxy, and NR11R12; R11 and R12 =H, C1-C6 alkyl, C2-C6 alkanoyl, C1-C6 alkanoyl substituted with from one to three groups selected from nitro, halo(F, Cl, Br, I), C1-C4-alkoxy, and amino, and C6-C12-aryl-C1-C8-alkyl where the aryl group is opt. substituted with 1-3 of nitro, halo(F, Cl, Br, I), and C1-C4-alkoxy; R13 = H, C1-C6 alkyl, halo(F, Cl, Br, I)-C1-C6 alkyl, phenyl, benzyl, and CH2-O-COCH3; R15 = C6-C14aryl, heteroaryl, where the heteroaryl is a 5- or 6-member aromatic ring containing 1 to 3 heteroatoms selected from O, N, and S and where the heteroaryl is opt. substituted with one or two substituents from OH, SH, C1-C4alkyl, C1-C4alkoxy, CF3, halo(F, Cl, Br, I), NO2, COOH, COO-(C1-C4alkyl), NH2, NH(C1-C4alkyl), and N(C1-C4alkyl)2, C3-C7-cycloalkyl, C1-C4-alkyl, unsubstituted or substituted with a substituent selected from the group C6-C14aryl, heteroaryl as defined above, OH, SH, C1-C4-alkyl, C1-C4-alkoxy, C1-C4-alkylthio, CF3, halo(F, Cl, Br, I), NO2, CO2H, CO2-(C1-C4)-alkyl, NH2, N[(C1-C4)-alkyl]2, NH[(C1-C4)-alkyl], PO3H, and PO(OH)(C1-C4)-alkoxy, and (C1-C4)-perfluoroalkyl; R16 = CN, NO2, COOR13, C1-C6-perfluoroalkyl, and CF3; R19 = H, C1-C6alkyl, C2-C6alkenyl, C1-C6alkoxy, C2-C6alkoxyalkyl, CH2-O-COCH3, and benzyl, where the phenyl moiety is opt. substituted with NO2, NH2, OH, and OCH3; X = NR24-C(=O)-R25, NR24-CH(OH)-R25, and NR24-S(O)u-R25 where u is 0, 1, or 2, R24 = C1-C6alkyl, and halo(F, Cl, Br, I)C1-C6alkyl; R25 = R25', (vii) or (viii); R25' = C1-C6alkyl, C2-C6alkenyl, C1-C6alkylamine, C2-C6alkenylamine, and halo(F, Cl, Br, I)C1-C6alkyl

where any alkyl or alkenyl moiety is substituted with NR27R28 and one or more groups selected from SH and SSR26; R26 = C1-C6alkyl, halo(F, Cl, Br, I)C1-C6alkyl, and C1-C6alkanoyl; R27 and R28 = H, C1-C6alkyl, phenyl, naphthyl, benzyl, CH2naphthyl (a or b), C1-C6alkanoyl, C1-C6cycloalkanoyl, C6-C10aroyl, C6-C10arylC1-C6alkanoyl, C1-C6alkylsulfonyl, C6-C10arylsulfonyl, C6-C10arylC1-C6alkylcarbamoyl, cinnamoyl, heterocyclecarbonyl, C1-C6alkoxycarbonyl, C6-C10aryloxycarbonyl, C6-C10arylC1-C6alkoxycarbonyl, and pyroglutamyl;NR27R28 = (ix) or (x); G = -CH2-, O, S(O)u where u is 0, 1, or 2, and NR28; J-M is selected from C2-C4alkylene and C2-C4alkenylene; R29 H, C1-C3alkyl; and

pharmaceutically acceptable salts thereof.

Dwg.0/7

L136 ANSWER 4 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1994-083105 [10] WPIX
CR 1991-339750 [46]; 1995-206308 [27]; 1996-497642 [49]
DNC C1994-038069
TI New **farnesyl-transferase** inhibitors - used for inhibiting attachment of a **farnesyl** moiety to a p21ras protein in malignant cells.
DC B04 D16
IN **BROWN, M S**; **GOLDSTEIN, J L**; MARSTERS, J C; **REISS, Y**; MARSTERS, J
PA (TEXA) UNIV TEXAS SYSTEM; (GETH) GENENTECH INC
CYC 45
PI WO 9404561 A1 19940303 (199410)* EN 183 C07K005-10
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN
AU 9348391 A 19940315 (199428) C07K005-10
EP 656903 A1 19950614 (199528) EN C07K005-10
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 08500828 W 19960130 (199642) 181 C07K005-103

US 6083917 A 20000704 (200036) A61K038-00
ADT WO 9404561 A1 WO 1993-US8062 19930824; AU 9348391 A AU 1993-48391 19930824; EP 656903 A1 EP 1993-921209 19930824, WO 1993-US8062 19930824; JP 08500828 W WO 1993-US8062 19930824, JP 1994-506619 19930824; US 6083917 A **CIP of US 1990-510706 19900418, CIP of US 1990-615715 19901120**, CIP of US 1992-822011 19920116, US 1992-935087 19920824
FDT AU 9348391 A Based on WO 9404561; EP 656903 A1 Based on WO 9404561; JP 08500828 W Based on WO 9404561; US 6083917 A CIP of US 5141851
PRAI US 1992-935087 19920824; **US 1990-510706 19900418; US 1990-615715 19901120**; US 1992-822011 19920116
REP EP 461869; EP 523873; WO 9116340
IC ICM A61K038-00; C07K005-10; C07K005-103
ICS A61K037-02; A61K038-02; A61K038-55; C07K005-00; C07K005-117; C07K007-00; C07K007-02; C07K007-06; C07K007-08; C12N009-99
ICA C12N009-10; C12N015-09
AB WO 9404561 A UPAB: 20020128
A pure **farnesyltransferase** (FT) inhibitor comprises a cpd. having a FT inhibitor peptide sequence within its structure, the sequence being capable of inhibiting the **farnesylation** of p21ras by protein FT without itself serving as a substrate for **farnesylation** by the enzyme, the FT inhibitor sequence being defined as including the amino acids CA1A2X (where C = cysteine, A1 = any aliphatic, aromatic or hydroxy amino acid; A2 = any aromatic amino acid or amino acid modified to incorporate one or more aromatic moieties, X = met, ser, glu or cys) whereby when the cpd. is introduced intracellularly into a target cell, the inhibitor is provided in a form where the C residue of CA1A2X is a positively charged amino terminus of the inhibitor. The inhibitor may be capable of being modified by hydrolysis, deacylation or enzymatic action to reveal an N-terminal cysteine having the positively charged alpha nitrogen.
USE/ADVANTAGE - The FT inhibitors do not act as a substrate for **farnesylation** by the enzyme so that they are not consumed by the inhibition process. The FT inhibitors are used for inhibiting the attachment of a **farnesyl** moiety to a p21ras protein in malignant cells (claimed) for the treatment of cancer.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-M01; B14-H01; D05-H17A6

L136 ANSWER 5 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1991-370840 [51] WPIX
DNC C1991-159856
TI New tetra peptide inhibitors of Ras protein **farnesylation** - prevent the transformation of normal cells into cancer cells.
DC B04
IN DIXON, R A F; GARSKY, V M; GIBBS, J B; SCHRABER, M D
PA (GIBB-I) GIBBS J B; (MERI) MERCK & CO INC
CYC 9
PI EP 461869 A 19911218 (199151)*
R: CH DE FR GB IT LI NL
CA 2044333 A 19911213 (199210)
JP 04243893 A 19920831 (199242) 7 C07K005-10
EP 461869 A3 19920708 (199334)
ADT EP 461869 A EP 1991-305283 19910612; JP 04243893 A JP 1991-140295 19910612; EP 461869 A3 EP 1991-305283 19910612
PRAI **US 1990-536840 19900612**; US 1991-700232 19910517
REP NoSR.Pub; 4.Jnl.Ref; EP 203587; EP 456180; WO 9116340
IC ICM C07K005-10
ICS A61K037-02; C07K015-00
AB EP 461869 A UPAB: 19931119

(A) A tetrapeptide which inhibits plasma membarne Ras protein localisation and prevents transformation of normal cells into cells is claimed, comprising the amino acid sequence cys-Aaa1-Aaa2-Xaa (I) (where Aaa1, Aaa2 = aliphatic amino acids, e.g. Ala, Val, Leu or Ile; Xaa = any amino acid, e.g. Ser or Met).

(B) Also claimed is the use of a cpd. as in (A) for the mfr. of a medicament for inhibiting **farnesylation** of Ras protein.

(C) Also claimed is a cpd. as in (A) which inhibits plasma membrane Ras protein localisation and prevents transformation of normal cells into cancer cells, which cpd. has the sequence S-(trans,trans)**farnesyl** - Cy-Aaa1-Aaa2-Xaa (II).

USE - The cpds. and their analogues are inhibitors of **farnesyl-protein transferase.** Administration of the cpds. to block Ras **farnesylation** not only decreases the amount of Ras in the membrane but also generates a cytosolic pool of Ras. Inhibition of Ras protein **farnesylation** blocks the ability of Ras to transform normal cells to cancer cells. @(7pp Dwg.No.0/0 0/0

FS CPI
FA AB; DCN
MC CPI: B04-C01A; B12-G01B2; B12-G07

L136 ANSWER 6 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1991-339750 [46] WPIX
CR 1994-083105 [10]; 1995-206308 [27]; 1996-497642 [49]
DNC C1991-146680
TI Compsn. comprising purified **farnesyl-protein transferase** - used to inhibit attachment of **farnesyl** moiety to RAS protein in malignant cells and to treat cancer.
DC B04 D16
IN **BROWN, M S; GOLDSTEIN, J L; REISS, Y**
PA (TEXA) UNIV TEXAS SYSTEM
CYC 35
PI WO 9116340 A 19911031 (199146)* 87
RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE
W: AT AU BB BG BR CA CH DE DK ES FI GB HU JP KP KR LK LU MC MG MW NL NO PL RO SD SE SU US
AU 9176946 A 19911111 (199207)
US 5141851 A 19920825 (199237) 24 C12Q001-48 <--
EP 528820 A1 19930303 (199309) EN 87 C07K007-06
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
AU 637497 B 19930527 (199328) C07K015-06
JP 05506779 W 19931007 (199345) C12N009-10 <--
EP 528820 B1 19961009 (199645) EN 43 C07K007-06
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69122611 E 19961114 (199651) C07K007-06
EP 528820 B2 20011219 (200206) EN C07K007-06
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
CA 2076652 C 20030610 (200345) EN C12N015-54
US 2003170766 A1 20030911 (200367) C12Q001-48 <--
US 6632626 B1 20031014 (200368) C12Q001-48 <--
ADT US 5141851 A **CIP of US 1990-510706 19900418, US 1990-615715 19901120**; EP 528820 A1 EP 1991-907853 19910418, **WO 1991-US2650 19910418**; AU 637497 B AU 1991-76946 19910418; JP 05506779 W JP 1991-507785 19910418, **WO 1991-US2650 19910418**; EP 528820 B1 EP 1991-907853 19910418, **WO 1991-US2650 19910418**; DE 69122611 E DE 1991-622611 19910418, EP 1991-907853 19910418, **WO 1991-US2650 19910418**; EP 528820 B2 EP 1991-907853 19910418, **WO 1991-US2650 19910418**; CA 2076652 C CA 1991-2076652 19910418, **WO 1991-US2650 19910418**; US 2003170766 A1 **CIP of US 1990-510706 19900418, CIP of US 1990-615715 19901120, Cont of WO 1991-US2650 19910418, Cont of US 1992-937893 19921222**, US 2002-83894 20020227; US 6632626 B1 **CIP of US 1990-510706 19900418, CIP**

**of US 1990-615715 19901120, Div ex US 1992-937893 19921222,**
US 2000-665362 20000919

FDT EP 528820 A1 Based on WO 9116340; AU 637497 B Previous Publ. AU 9176946, Based on WO 9116340; JP 05506779 W Based on WO 9116340; EP 528820 B1 Based on WO 9116340; DE 69122611 E Based on EP 528820, Based on WO 9116340; EP 528820 B2 Based on WO 9116340; CA 2076652 C Based on WO 9116340; US 2003170766 A1 CIP of US 5141851; US 6632626 B1 CIP of US 5141851

PRAI **US 1990-615715 19901120; US 1990-510706 19900418; WO 1991-US2650 19910418; US 1992-937893 19921222;** US 2002-83894 20020227; US 2000-665362 20000919

REP 8.Jnl.Ref; 6.Jnl.Ref

IC ICM C07K007-06; C07K015-06; **C12N009-10**; C12N015-54; **C12Q001-48**
ICS A61K037-02; A61K037-52; A61K037-64; A61K038-00; A61K038-07; A61K038-08; C07K004-00; C07K005-10; C07K013-00; C12N005-06; C12P021-02

AB WO 9116340 A UPAB: 20031022
Enzyme has the following characteristics: (a) capable of catalysing the transfer of **farnesol** to a protein or peptide having a **farnesyl** acceptor moiety; (b) capable of binding to an affinity chromatography medium comprising TKCVIM coupled to a matrix; (c) mol.weight of 70,000-100,000 kD from gel filtration chromatrography, and has two different subunits each of mo weight 45,000-50,000 kD on SDS-PAGE; and (d) having **farnesyl transferase** activity that is inhibited by TKCVIM, CVIM or KKSKTKCVIM. Also claimed are preparation of enzyme, assaying the enzyme activity, a **farnesyl transferase** inhibitor, DNA encoding either subunit of the enzyme and a recombinant vector comprising the DNA.

USE/ADVANTAGE - Used to inhibit the attachment of a **farnesyl** moiety to a RAS protein in malignant cells, and therefore to treat cancer. Assaying the ability of a substance to inhibit **farnesyl transferase** activity is also provided.

Dwg.0/17

FS CPI

FA AB; DCN

MC CPI: B04-B02C4; B04-B04A; B04-C01; B10-E04D; B11-C08E3; B12-G07; **B12-K04**; **D05-C03D**; D05-H12

ABEQ US 5141851 A UPAB: 19930928
Compsn. comprises an isolated **farnesyl:-protein transferase** which: (a) catalyses the transfer of all-trans **farnesyl** protein or peptide having a C-terminal **farnesyl** acceptor moiety. (b) binds to an affinity chromatography medium comprised of Thr-Lys-Cys-Val-Ile-Met coupled to a matrix. (c) has a mol. wt. of 70,000-100,000 kD on gel filtration chromatography and has two sub-units of 45,000-50,000 kD on SDS-PAGE. (d) is inhibited by Thr-Lys-Cys-Val-Ile-Met, Cys-Val-Ile-Met or Lys-Lys-Ser-Lys-Thr-Lys-Cys-Val-Ile-Met.

USE/ADVANTAGE - Used in screening for identifying anticancer agents which inhibit the enzyme, esp. the p21 ras proteins. Also for treating e.g. ras-related cancers.

0/15

ABEQ EP 528820 B UPAB: 19961111
A composition comprising a purified mammalian **farnesyl: protein transferase** enzyme, characterised as follows: (a) capable of catalysing the transfer of **farnesol** to a protein or peptide having a **farnesyl** acceptor moiety; (b) capable of binding to an affinity chromatography medium comprised of TKCVIM coupled to a suitable matrix; (c) exhibiting a molecular weight of between 70,000 Da and 100,000 Da upon gel filtration chromatography, and comprised of two different subunits, each exhibiting a molecular weight of approximately 45,000 Da to 50,000 Da upon SDS-PAGE; and (d) having a **farnesyl transferase** activity that is capable of being inhibited by TKCVIM; CVIM; or KKSKTKCVIM.

Dwg.0/17

L136 ANSWER 7 OF 7 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1991-334169 [46] WPIX
DNC C1991-144175
TI Assaying **farnesyl-protein transferase** - by measuring incorporation of **farnesyl** residues into ras protein substrate, identifying cpds. which block neoplastic transformation.
DC B04 D16
IN BARBACID, M; MANNE, V
PA (BARB-I) BARBACID M; (SQUI) SQUIBB & SONS INC E R
CYC 7
PI EP 456180 A 19911113 (199146)*
R: DE FR GB IT
CA 2040529 A 19911109 (199205)
JP 04228099 A 19920818 (199240) 16 C12Q001-48 <--
US 5185248 A 19930209 (199308) 17 C12Q001-48 <--
EP 456180 B1 19980304 (199813) EN 22 C12N009-10 <--
R: DE FR GB IT
DE 69128977 E 19980409 (199820) C12N009-10 <--
JP 3280042 B2 20020430 (200230) 15 C12Q001-48 <--
JP 2002159300 A 20020604 (200239) 15 C12Q001-48 <--
ADT EP 456180 A EP 1991-107390 19910507; JP 04228099 A JP 1991-102633 19910508; US 5185248 A **US 1990-520570 19900508**; EP 456180 B1 EP 1991-107390 19910507; DE 69128977 E DE 1991-628977 19910507, EP 1991-107390 19910507; JP 3280042 B2 JP 1991-102633 19910508; JP 2002159300 A Div ex JP 1991-102633 19910508, JP 2001-342998 19910508
FDT DE 69128977 E Based on EP 456180; JP 3280042 B2 Previous Publ. JP 04228099
PRAI **US 1990-520570 19900508**
REP 5.Jnl.Ref
IC ICM **C12N009-10**; **C12Q001-48**
ICS G01N033-68
AB EP 456180 A UPAB: 19930928
Assay for **farnesyl-protein transferase** (FPT) activity comprises (a) reacting a protein/peptide substrate (A) containing a CAAX motif, with **farnesyl** pyrophosphate (FPP) in presence of test sample, and (b) determining whether the **farnesyl** residue becomes incorporated into (A).
The method is also used to detect cpds. (I) which can inhibit ras oncogene activity (such cpds. reduce incorporation of **farnesyl** residues into (A) relative to a similar test without (I)).
Also new are (1) kits for identification of (I) or (2) purified FPT.
USE/ADVANTAGE - (I) which can be identified by the assay are useful for blocking neoplastic transformations mediated by the ras oncogene. They do not interfere with other metabolic pathways which use FPP as an intermediate.
0/10
FS CPI
FA AB; DCN
MC CPI: B04-B02C4; B04-B04A6; B04-C01; B05-A01B; B05-A03; B05-B01P; B10-E03; B11-C07B; B11-C08D1; **B12-K04**; D05-A02C; **D05-H09**; D05-H13
ABEQ US 5185248 A UPAB: 19930928
Assay for identifying cpds. that inhibit ras oncogene activity comprises: (a) reacting a protein or peptide substrate having a CAAX motif with **farnesyl** pyrophosphate and **farnesyl-protein transferase** in the presence of a test substance; and (b) detecting whether the **farnesyl** residue is incorporated into the protein or peptide substrate, in which the ability of the test substance to inhibit ras is indicated by a decrease in incorporation of **farnesyl** residues compared to that incorporated in the absence of the rest.
USE/ADVANTAGE - Assaying for substances that block **farnesylation** of ras oncogene products e.g. those which inhibit

ras-mediated transformation but do not cause major disruptions of important cell pathways that require **farnesyl-protein transferase** as an intermediate.
0/10

ABEQ EP 456180 B UPAB: 19980330
Assay for **farnesyl-protein transferase** (FPT) activity comprises (a) reacting a protein/peptide substrate (A) contg. a CAAX motif, with **farnesyl** pyrophosphate (FPP) in presence of test sample, and (b) determining whether the **farnesyl** residue becomes incorporated into (A).
The method is also used to detect cpds. (I) which can inhibit ras oncogene activity (such cpds. reduce incorporation of **farnesyl** residues into (A) relative to a similar test without (I)).
Also new are (1) kits for identification of (I) or (2) purified FPT.
USE/ADVANTAGE - (I) which can be identified by the assay are useful for blocking neoplastic transformations mediated by the ras oncogene. They do not interfere with other metabolic pathways which use FPP as an intermediate.
Dwg.0/10

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=> d his

     (FILE 'HOME' ENTERED AT 13:34:50 ON 25 MAY 2004)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:34:58 ON 25 MAY 2004
L1           780 S ?FARNESYL?/CNS
L2           239 S L1 AND ?TRANSFERASE?/CNS
L3           541 S L1 NOT L2
L4           206 S L2 AND FARNES?/INS.HP
L5            33 S L2 NOT L4
L6            22 S L5 AND FARNESYLTRANSFERASE
L7            11 S L6 AND CYSTEINE
L8             6 S L7 NOT CANDIDA
L9           172 S L4 AND FARNESYLTRANSFERASE/INS.HP
L10           34 S L4 NOT L9
L11            5 S L10 AND FARNESYL PROTEIN TRANSFERASE
L12          183 S L9,L8,L11
L13           29 S L10 NOT L12
L14           29 S L4 NOT L12
L15           29 S L13,L14
L16            4 S L15 AND FARNESYL TRANSFERASE
L17            0 S L15 AND FARNESYLTRANSFERASE
L18            0 S L15 AND FARNESYL PROTEIN TRANSFERASE
L19          187 S L12,L16
L20           25 S L15 NOT L19
L21          593 S L1-L18,L20 NOT L19

     FILE 'HCAPLUS' ENTERED AT 13:42:56 ON 25 MAY 2004
L22         1800 S L19
L23         6717 S L21
L24         1909 S ?FARNESYLTRANSFERASE? OR ?FARNESYL PROTEIN TRANSFERASE?
L25          612 S FARNESYL TRANSFERASE
L26         8806 S L22-L25
L27          201 S L26 AND (DRUG SCREENING+OLD,NT,PFT OR DRUG DESIGN+OLD,NT,PFT)
                 E REISS Y/AU
L28           39 S E3,E4
                 E GOLDSTEIN J/AU
L29          257 S E3,E12,E13
                 E GOLDSTEIN JOE/AU
L30            4 S E3
L31          425 S E27,E28,E31
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                E BROWN M/AU
L32          263 S E3,E49
                E BROWN MICHAEL/AU
L33          105 S E3
                E BROWN MICHAEL S/AU
L34          448 S E3-E5
L35            8 S E16,E17
L36           41 S L26 AND L28-L35
L37            5 S L28-L35 AND (TKCVIM OR CVIM OR KKSKTKCVIM)
L38            5 S L28-L35 AND ?CVIM?
L39            5 S L37,L38

     FILE 'REGISTRY' ENTERED AT 13:50:31 ON 25 MAY 2004
                E CVIM/SQEP
L40           29 S E3
                E TKCVIM/SQEP
L41            2 S E3
                E KKSKTKCVIM/SQEP
L42            3 S E3

     FILE 'HCAPLUS' ENTERED AT 13:51:24 ON 25 MAY 2004
L43           45 S L40-L42
L44           30 S TKCVIM OR CVIM OR KKSKTKCVIM
L45           60 S L43,L44 AND L26
L46          137 S L26 AND P21RAS
L47           24 S L26 AND P21 RAS
L48         1361 S L26 AND RAS
L49          309 S L26 AND P21?
L50           26 S L36 AND L45,L46-L49
L51           26 S L39,L50
L52            1 S L51 AND L27
L53            5 S L51 AND SCREEN?
L54           18 S L51 AND INHIBIT?
L55           18 S L52-L54
L56           18 S L39,L55
L57           23 S L36 NOT L56
L58           18 S L56 AND (INHIBIT? OR BLOCK? OR ANTAGON? OR PREVENT?)
L59            5 S L58 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L60           13 S L58 NOT L59
L61            4 S (US20030170766 OR US5141851)/PN OR (US2000-665637# OR US92-93
L62            4 S L61 AND L22-L39,L43-L60
L63            5 S L59,L62
L64         8921 S L26 OR ?FARNESYL?(L)?TRANSFERASE?
L65         2692 S L64 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L66            6 S L65 AND L43,L44
L67           11 S L65 AND (P21? OR P21 RAS)
L68           13 S L65 AND RAS PROTEINS+OLD,NT,PFT/CT
L69            1 S L65 AND (DRUG SCREENING+OLD,NT,PFT OR DRUG DESIGN+OLD,NT,PFT)
L70          494 S L65 AND (INHIBIT? OR BLOCK? OR ANTAGON? OR PREVENT?)
L71           37 S L70 AND METHOD?
L72           48 S L63,L66-L69,L71
L73           16 S L72 AND ENZYM?/SC,SX
                SEL DN AN L73 7 12 13 14 16
L74           11 S L73 NOT E1-E15
L75           32 S L72 NOT L73
L76           11 S L74 AND (RAS OR P21? OR ?FARNES? OR ?TRANSFERASE? OR ?CVIM? O
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:14:41 ON 25 MAY 2004
L77           24 S E16-E39
L78           18 S L77 AND L1-L21
L79            6 S L77 AND L40-L42
L80            3 S L78 AND UNSPECIFIED NOT SQL/FA
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L81          15 S L78 NOT L79,L80

     FILE 'REGISTRY' ENTERED AT 14:16:43 ON 25 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 14:36:16 ON 25 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 14:37:10 ON 25 MAY 2004
L82           6 S L67,L68 NOT L76

     FILE 'CANCERLIT' ENTERED AT 14:38:22 ON 25 MAY 2004
L83         570 S L24 OR L25
L84           0 S L19
L85         152 S L21
L86          14 S L83,L85 AND PY<=1990

     FILE 'MEDLINE' ENTERED AT 14:40:39 ON 25 MAY 2004
L87        1177 S L24 OR L25
L88         895 S L21
L89         293 S L87,L88 AND PY<=1990
L90          18 S L89 AND AI/CT
L91           3 S L90 AND TRANSFERASES(L)AI/CT
L92          15 S L90 NOT L91
L93         275 S L89 NOT L90
L94          11 S L93 AND (RAS OR P21?)
L95           5 S L93 AND C4./CT
                E DRUG SCREENING/CT
                E E4+ALL
L96          11 S L93 AND E15+NT
L97          25 S L94-L96

     FILE 'BIOSIS' ENTERED AT 14:43:54 ON 25 MAY 2004
                E BROWN M/AU
L98         990 S E3
                E BROWN M S/AU
L99         519 S E3,E4
                E BROWN MICHAEL/AU
L100        178 S E3,E21
L101          4 S E37
                E GOLDSTEIN J/AU
L102        845 S E3,E14
                E GOLDSTEIN JOE/AU
L103        122 S E19,E22
                E REISS Y/AU
L104         30 S E3,E4
L105         32 S L26 AND L98-L104
L106          4 S L105 AND PY<=1990
L107          5 S L105 NOT (P OR ARTICLE)/DT
L108          8 S L106,L107
                SEL DN AN 5 6 7
L109          3 S L108 AND E1-E9

     FILE 'BIOSIS' ENTERED AT 14:46:27 ON 25 MAY 2004

     FILE 'WPIX' ENTERED AT 14:46:45 ON 25 MAY 2004
L110        617 S L24/BIX OR L25/BIX
L111          4 S L61
L112       2606 S C12N009-10/IC,ICM,ICS
L113       2193 S C12Q001-48/IC,ICM,ICS
L114          2 S L111 AND L112,L113
L115          4 S L111,L114
                E BROWN M/AU
L116        200 S E3,E24
                E GOLDSTEIN J/AU
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L117        107 S E3,E11
                E REISS Y/AU
L118         10 S E3
L119          5 S L110,L112,L113 AND L116-L118
L120          5 S L115,L119
L121        708 S L110,L112-L113 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L122        197 S L121 AND (N102 (S) P831 (S) Q233)/M0,M1,M2,M3,M4,M5,M6
L123        259 S L121 AND (P831 (S) Q233)/M0,M1,M2,M3,M4,M5,M6
L124        305 S L121 AND (D05-H09 OR B12-K04 OR C12-K04 OR B12-K04E OR C12-K0
L125        357 S L122-L124
L126       1607 S D05-C03D/MC
L127        235 S L126 AND (PY<=1990 OR PRY<=1990 OR AY<=1990)
L128         35 S L127 AND (P831 (S) Q233)/M0,M1,M2,M3,M4,M5,M6
L129         17 S L127 AND (N102 (S) P831 (S) Q233)/M0,M1,M2,M3,M4,M5,M6
L130         31 S L127 AND (D05-H09 OR B12-K04 OR C12-K04 OR B12-K04E OR C12-K0
L131        384 S L125,L128-L130
L132          4 S L131 AND ?FARNES?/BIX
L133          3 S L132 NOT PRENYL/TI
L134          6 S L121,L127 AND L110
L135          6 S L134 AND ?FARNES?/BIX
L136          7 S L120,L133-L135

     FILE 'WPIX' ENTERED AT 15:18:37 ON 25 MAY 2004

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